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Barb O'Boyer

follow up

96186 Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Rebecca Kosht Examiner # : _____ Date: 6/9/03
Art Unit: 1614 Phone Number 30 8 4724 Serial Number: 10/036205
Mail Box and Bldg/Room Location: CM1 2D01 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Lowering Glycosylated Hb

Inventors (please provide full names): Hiroyuki Odaka

M Yamane

Earliest Priority Filing Date: _____

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search agnst categories of Claim 23 Dec & "anorectic" Dec any of them used to treat diabetes

Thanks

Rebecca

Provide structures where possible

Rush Search Appreciated

TC 1600 SPE A.U 1615

****

STAFF USE ONLY

Searcher: BOB
Searcher Phone #: _____
Searcher Location: _____
Date Searcher Picked Up: _____
Date Completed: 6-12-03
Searcher Prep & Review Time: 35
Clerical Prep Time: _____
Online Time: 93

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) _____
Bibliographic 8
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

STN 438
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 96186

TO: Rebecca Cook **Location: CM1/2B07/2D01** **Art Unit: 1614** **Thursday, June 12, 2003** **Case Serial Number: 036208**	**From: Barb O'Bryen** **Location: Biotech-Chem Library** **CM1-6A05** **Phone: 308-4291** 1308 **barbara.obryen@uspto.gov**

Search Notes

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact:***

Mary Hale, Information Branch Supervisor
308-4258, CM1-1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk

```
=> fil reg
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STRUCTURE FILE UPDATES:   11 JUN 2003  HIGHEST RN 529474-19-9
DICTIONARY FILE UPDATES:  11 JUN 2003  HIGHEST RN 529474-19-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide l4

L4   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   169494-85-3  REGISTRY
CN   Leptin (9CI)  (CA INDEX NAME)
ENTE A proteinaceous hormone from the obese gene that regulates food intake,
     energy expenditure, and body weight
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
       BIOSIS, CA, CAPLUS, CBNB, CEN, CHEMCATS, CIN, IPA, PROMT, TOXCENTER,
       USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            5239 REFERENCES IN FILE CA (1957 TO DATE)
              77 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            5274 REFERENCES IN FILE CAPLUS (1957 TO DATE)


=> d ide l6

L6   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   391975-82-9  REGISTRY
CN   Corticotropin releasing factor (human) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   GenBank V00571-derived protein GI 35356
FS   PROTEIN SEQUENCE
DR   431542-37-9
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
              2 REFERENCES IN FILE CA (1957 TO DATE)
```

2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

intentionally blank

```
=> fil capl; d que 123; d que 133; d que 136; d que 137; d que 143
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FILE COVERS 1907 - 12 Jun 2003  VOL 138 ISS 24
FILE LAST UPDATED: 11 Jun 2003  (20030611/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L7          1824 SEA FILE=CAPLUS ABB=ON  APPETITE DEPRESSANTS+OLD/CT
L22            8 SEA FILE=CAPLUS ABB=ON  TRIPEPTIDYLPEPTIDASE(W)(II OR 2)
L23            1 SEA FILE=CAPLUS ABB=ON  L7 AND L22


L7          1824 SEA FILE=CAPLUS ABB=ON  APPETITE DEPRESSANTS+OLD/CT
L19          517 SEA FILE=CAPLUS ABB=ON  (MELANIN OR MELANOPHORE OR MELANOSOME)(
               W)CONCENTRATING/OBI
L21          143 SEA FILE=CAPLUS ABB=ON  (PROCOLIPASE OR ENTEROSTATIN)/OBI
L26        42315 SEA FILE=CAPLUS ABB=ON  AGONIST#/OBI
L30           12 SEA FILE=CAPLUS ABB=ON  L19(L)L26
L32            2 SEA FILE=CAPLUS ABB=ON  L21(L)L26
L33            2 SEA FILE=CAPLUS ABB=ON  L7 AND (L30 OR L32)


L7          1824 SEA FILE=CAPLUS ABB=ON  APPETITE DEPRESSANTS+OLD/CT
L15         6847 SEA FILE=CAPLUS ABB=ON  NEUROPEPTIDE Y/OBI
L16         9872 SEA FILE=CAPLUS ABB=ON  CHOLECYSTOKININ/OBI
L17         2120 SEA FILE=CAPLUS ABB=ON  GALANIN/OBI
L20         1030 SEA FILE=CAPLUS ABB=ON  MELANOCORTIN/OBI
L25       806180 SEA FILE=CAPLUS ABB=ON  ANTAGONIST#/OBI OR INHIBIT?/OBI
L26        42315 SEA FILE=CAPLUS ABB=ON  AGONIST#/OBI
L27          925 SEA FILE=CAPLUS ABB=ON  L15(L)L25
L28          302 SEA FILE=CAPLUS ABB=ON  L16(L)L26
L29          322 SEA FILE=CAPLUS ABB=ON  L17(L)L25
L31          141 SEA FILE=CAPLUS ABB=ON  L20(L)L26
L36            2 SEA FILE=CAPLUS ABB=ON  L7 AND L27 AND L28 AND L29 AND L31


L4             1 SEA FILE=REGISTRY ABB=ON  LEPTIN/CN
L5           117 SEA FILE=REGISTRY ABB=ON  GLUCAGON-LIKE PEPTIDE 1?/CN
L6             1 SEA FILE=REGISTRY ABB=ON  "CORTICOTROPIN RELEASING FACTOR
               (HUMAN)"/CN
L7          1824 SEA FILE=CAPLUS ABB=ON  APPETITE DEPRESSANTS+OLD/CT
```

```
L12        5857 SEA FILE=CAPLUS ABB=ON  L4 OR LEPTIN#/OBI
L13        1237 SEA FILE=CAPLUS ABB=ON  L5 OR GLUCAGON LIKE PEPTIDE(W)(I OR
                1)/OBI
L14        5850 SEA FILE=CAPLUS ABB=ON  L6 OR CORTICOTROPIN RELEASING/OBI
L37           4 SEA FILE=CAPLUS ABB=ON  L12 AND L13 AND L14 AND L7


L4            1 SEA FILE=REGISTRY ABB=ON  LEPTIN/CN
L5          117 SEA FILE=REGISTRY ABB=ON  GLUCAGON-LIKE PEPTIDE 1?/CN
L6            1 SEA FILE=REGISTRY ABB=ON  "CORTICOTROPIN RELEASING FACTOR
                (HUMAN)"/CN
L7         1824 SEA FILE=CAPLUS ABB=ON  APPETITE DEPRESSANTS+OLD/CT
L8        12265 SEA FILE=CAPLUS ABB=ON  ANTIDIABETIC AGENTS+OLD/CT
L9        48785 SEA FILE=CAPLUS ABB=ON  DIABETES MELLITUS/CT
L12        5857 SEA FILE=CAPLUS ABB=ON  L4 OR LEPTIN#/OBI
L13        1237 SEA FILE=CAPLUS ABB=ON  L5 OR GLUCAGON LIKE PEPTIDE(W)(I OR
                1)/OBI
L14        5850 SEA FILE=CAPLUS ABB=ON  L6 OR CORTICOTROPIN RELEASING/OBI
L15        6847 SEA FILE=CAPLUS ABB=ON  NEUROPEPTIDE Y/OBI
L16        9872 SEA FILE=CAPLUS ABB=ON  CHOLECYSTOKININ/OBI
L17        2120 SEA FILE=CAPLUS ABB=ON  GALANIN/OBI
L20        1030 SEA FILE=CAPLUS ABB=ON  MELANOCORTIN/OBI
L25      806180 SEA FILE=CAPLUS ABB=ON  ANTAGONIST#/OBI OR INHIBIT?/OBI
L26       42315 SEA FILE=CAPLUS ABB=ON  AGONIST#/OBI
L27         925 SEA FILE=CAPLUS ABB=ON  L15(L)L25
L28         302 SEA FILE=CAPLUS ABB=ON  L16(L)L26
L29         322 SEA FILE=CAPLUS ABB=ON  L17(L)L25
L31         141 SEA FILE=CAPLUS ABB=ON  L20(L)L26
L39          16 SEA FILE=CAPLUS ABB=ON  L7 AND (L12 OR L13 OR L14) AND (L27 OR
                L28 OR L29 OR L31) AND (L8 OR L9)
L43           3 SEA FILE=CAPLUS ABB=ON  L39 AND (DIABETES OR Y)/TI


=> s l23 or l33 or l36 or l37 or l43

L224          8 L23 OR L33 OR L36 OR L37 OR L43

=> fil medl; d que l69; d que l74; d que l76; d que l80

FILE 'MEDLINE' ENTERED AT 11:31:06 ON 12 JUN 2003

 FILE LAST UPDATED: 11 JUN 2003 (20030611/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L58         149 SEA FILE=MEDLINE ABB=ON  NEUROPEPTIDE Y/CT(L)AI/CT
L59          31 SEA FILE=MEDLINE ABB=ON  CHOLECYSTOKININ+NT/CT(L)AG/CT
L60          10 SEA FILE=MEDLINE ABB=ON  GLUCAGON/CT(L)AG/CT
L63          39 SEA FILE=MEDLINE ABB=ON  GALANIN/CT(L)AI/CT
L65           1 SEA FILE=MEDLINE ABB=ON  (PROCOLIPASE OR ENTEROSTATIN)(3A)AGONI
                ST#
L66           1 SEA FILE=MEDLINE ABB=ON  TRIPEPTIDYLPEPTIDASE(W)(II OR
                2)(3A)(ANTAGONI? OR INHIBIT?)
L67        2593 SEA FILE=MEDLINE ABB=ON  APPETITE DEPRESSANTS/CT
```

AI = antagonists & inhibitors

AG = agonists

```
L68        2322 SEA FILE=MEDLINE ABB=ON  ANOREXIA/CT
L69           6 SEA FILE=MEDLINE ABB=ON  (L67 OR L68) AND ((L58 OR L59 OR L60)
                 OR L63 OR L65 OR L66)


L57        5092 SEA FILE=MEDLINE ABB=ON  LEPTIN/CT
L61        7135 SEA FILE=MEDLINE ABB=ON  CORTICOTROPIN-RELEASING HORMONE/CT
L67        2593 SEA FILE=MEDLINE ABB=ON  APPETITE DEPRESSANTS/CT
L68        2322 SEA FILE=MEDLINE ABB=ON  ANOREXIA/CT
L72        3196 SEA FILE=MEDLINE ABB=ON  (L57 OR L61)(L)(PD OR AD OR TU OR
                 PK)/CT
L74          13 SEA FILE=MEDLINE ABB=ON  (L67/MAJ OR L68/MAJ) AND L72/MAJ


L62        1301 SEA FILE=MEDLINE ABB=ON  GLUCAGON LIKE PEPTIDE(W)(1 OR I)
L64         436 SEA FILE=MEDLINE ABB=ON  (MELANIN OR MELANOPHORE OR MELANOSOME)
                 (W)CONCENTRATING(W)HORMONE#
L67        2593 SEA FILE=MEDLINE ABB=ON  APPETITE DEPRESSANTS/CT
L68        2322 SEA FILE=MEDLINE ABB=ON  ANOREXIA/CT
L76           2 SEA FILE=MEDLINE ABB=ON  L62 AND L64 AND (L67 OR L68)


L62        1301 SEA FILE=MEDLINE ABB=ON  GLUCAGON LIKE PEPTIDE(W)(1 OR I)
L64         436 SEA FILE=MEDLINE ABB=ON  (MELANIN OR MELANOPHORE OR MELANOSOME)
                 (W)CONCENTRATING(W)HORMONE#
L67        2593 SEA FILE=MEDLINE ABB=ON  APPETITE DEPRESSANTS/CT
L68        2322 SEA FILE=MEDLINE ABB=ON  ANOREXIA/CT
L78          16 SEA FILE=MEDLINE ABB=ON  (L62 OR L64) AND (L67/MAJ OR L68/MAJ)

L80           5 SEA FILE=MEDLINE ABB=ON  L78 AND GENERAL REVIEW/DT
```

PD = pharmacology
AD = administration & dosage
TU = Therapeutic use
PK = pharmacokinetics

```
=> s l69 or l74 or l76 or l80

L225         25 L69 OR L74 OR L76 OR L80

=> fil embase

FILE 'EMBASE' ENTERED AT 11:31:08 ON 12 JUN 2003
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 FILE COVERS 1974 TO 5 Jun 2003 (20030605/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

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=> d que l135; d que l142; d que l154

L102          2 SEA FILE=EMBASE ABB=ON  LEPTIN RECEPTOR AGONIST/CT
L104          3 SEA FILE=EMBASE ABB=ON  LEPTIN RESISTANCE/CT
L105         11 SEA FILE=EMBASE ABB=ON  NEUROPEPTIDE Y ANTAGONIST/CT
L106        256 SEA FILE=EMBASE ABB=ON  CHOLECYSTOKININ RECEPTOR STIMULATING
                 AGENT/CT
L108          2 SEA FILE=EMBASE ABB=ON  GLUCAGON LIKE PEPTIDE 1 AGONIST/CT
L110        379 SEA FILE=EMBASE ABB=ON  MELANIN CONCENTRATING HORMONE/CT
L111          1 SEA FILE=EMBASE ABB=ON  MELANOCORTIN AGONIST/CT
L114          1 SEA FILE=EMBASE ABB=ON  ENTEROSTATIN RECEPTOR AGONIST/CT
L115          1 SEA FILE=EMBASE ABB=ON  TRIPEPTIDYLPEPTIDASE/CT
```

```
L117       1316 SEA FILE=EMBASE ABB=ON  ANOREXIGENIC AGENT/CT
L135         15 SEA FILE=EMBASE ABB=ON  L117 AND (L102 OR (L104 OR L105 OR
                L106) OR L108 OR (L110 OR L111) OR (L114 OR L115))



L101       5382 SEA FILE=EMBASE ABB=ON  LEPTIN/CT
L103        813 SEA FILE=EMBASE ABB=ON  LEPTIN RECEPTOR/CT
L107        967 SEA FILE=EMBASE ABB=ON  GLUCAGON LIKE PEPTIDE 1/CT
L109      19375 SEA FILE=EMBASE ABB=ON  GLUCAGON/CT
L112        350 SEA FILE=EMBASE ABB=ON  MELANOCORTIN/CT
L113         93 SEA FILE=EMBASE ABB=ON  ENTEROSTATIN/CT
L116       7676 SEA FILE=EMBASE ABB=ON  CORTICOTROPIN RELEASING FACTOR/CT
L117       1316 SEA FILE=EMBASE ABB=ON  ANOREXIGENIC AGENT/CT
L136        863 SEA FILE=EMBASE ABB=ON  L117/MAJ
L140      24386 SEA FILE=EMBASE ABB=ON  L101/MAJ OR L103/MAJ OR L107/MAJ OR
                L109/MAJ OR L112/MAJ OR L113/MAJ OR L116/MAJ
L142          2 SEA FILE=EMBASE ABB=ON  L140 AND L136 AND GENERAL REVIEW/DT



L103        813 SEA FILE=EMBASE ABB=ON  LEPTIN RECEPTOR/CT
L107        967 SEA FILE=EMBASE ABB=ON  GLUCAGON LIKE PEPTIDE 1/CT
L109      19375 SEA FILE=EMBASE ABB=ON  GLUCAGON/CT
L112        350 SEA FILE=EMBASE ABB=ON  MELANOCORTIN/CT
L113         93 SEA FILE=EMBASE ABB=ON  ENTEROSTATIN/CT
L116       7676 SEA FILE=EMBASE ABB=ON  CORTICOTROPIN RELEASING FACTOR/CT
L117       1316 SEA FILE=EMBASE ABB=ON  ANOREXIGENIC AGENT/CT
L136        863 SEA FILE=EMBASE ABB=ON  L117/MAJ
L149         62 SEA FILE=EMBASE ABB=ON  (L103 AND (L107 OR L109 OR L112 OR
                L113 OR L116))
L150        219 SEA FILE=EMBASE ABB=ON  L107 AND (L109 OR L112 OR L113 OR
                L116)
L151         77 SEA FILE=EMBASE ABB=ON  L109 AND (L112 OR L113 OR L116)
L152         38 SEA FILE=EMBASE ABB=ON  L112 AND (L113 OR L116)
L153         11 SEA FILE=EMBASE ABB=ON  L113 AND L116
L154          7 SEA FILE=EMBASE ABB=ON  L136 AND (L149 OR L150 OR L151 OR L152
                OR L153)


=> s l135 or l142 or l154

L226         23 L135 OR L142 OR L154

=> fil wpids; d que l214; d que l220; s l214 or l220

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FILE LAST UPDATED:          9 JUN 2003      <20030609/UP>
MOST RECENT DERWENT UPDATE:     200336        <200336/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<
```

```
>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<

L189 .    12319 SEA FILE=WPIDS ABB=ON  AGONIST#
L195          3 SEA FILE=WPIDS ABB=ON  (MELANIN OR MELANOPHORE OR MELANOSOME)(W
              )CONCENTRATING HORMONE (3A)L189
L197          0 SEA FILE=WPIDS ABB=ON  (PROCOLIPASE OR ENTEROSTATIN)(3A)L189
L198          1 SEA FILE=WPIDS ABB=ON  (TRIPEPTIDYLPEPTIDASE OR (TRIPEPTIDYL
              OR TRI PEPTIDYL)(W)PEPTIDASE OR TRI(W)PEPTIDYPEPTIDASE)(W)(2
              OR II)
L200       4388 SEA FILE=WPIDS ABB=ON  ANORECT? OR APPETITE(2A)(DEPRESS? OR
              SUPPRESS?)
L214          3 SEA FILE=WPIDS ABB=ON  L200 AND (L195 OR L197 OR L198)



L187        326 SEA FILE=WPIDS ABB=ON  LEPTIN
L188     101859 SEA FILE=WPIDS ABB=ON  ANTAGONIST# OR INHIBITOR#
L189      12319 SEA FILE=WPIDS ABB=ON  AGONIST#
L190        135 SEA FILE=WPIDS ABB=ON  (NEUROPEPTIDE OR NEURO PEPTIDE)(W)Y(3A)L
              188
L191         37 SEA FILE=WPIDS ABB=ON  (CHOLECYSTOKININ)(3A)L189
L192        145 SEA FILE=WPIDS ABB=ON  GLUCAGON LIKE PEPTIDE(W)(1 OR I)
L193         30 SEA FILE=WPIDS ABB=ON  GALANIN(3A)L188
L194         25 SEA FILE=WPIDS ABB=ON  GLUCAGON(3A)L189
L195          3 SEA FILE=WPIDS ABB=ON  (MELANIN OR MELANOPHORE OR MELANOSOME)(W
              )CONCENTRATING HORMONE (3A)L189
L196         58 SEA FILE=WPIDS ABB=ON  MELANOCORTIN(3A)L189
L197          0 SEA FILE=WPIDS ABB=ON  (PROCOLIPASE OR ENTEROSTATIN)(3A)L189
L198          1 SEA FILE=WPIDS ABB=ON  (TRIPEPTIDYLPEPTIDASE OR (TRIPEPTIDYL
              OR TRI PEPTIDYL)(W)PEPTIDASE OR TRI(W)PEPTIDYPEPTIDASE)(W)(2
              OR II)
L199        232 SEA FILE=WPIDS ABB=ON  CORTICOTROPIN RELEASING
L219        332 SEA FILE=WPIDS ABB=ON  (ANORECT?/TI OR APPETITE/TI(2A)(DEPRESS?
              /TI OR SUPPRESS?/TI))
L220         10 SEA FILE=WPIDS ABB=ON  L219 AND (L187 OR (L190 OR L191 OR L192
              OR L193 OR L194 OR L195 OR L196 OR L197 OR L198 OR L199))



L227         13 L214 OR L220

=> dup rem l225,l224,l226,l227
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PROCESSING COMPLETED FOR L225
PROCESSING COMPLETED FOR L224
PROCESSING COMPLETED FOR L226
PROCESSING COMPLETED FOR L227
L228         68 DUP REM L225 L224 L226 L227 (1 DUPLICATE REMOVED)
```

ANSWERS '1-25' FROM FILE MEDLINE
ANSWERS '26-33' FROM FILE CAPLUS
ANSWERS '34-55' FROM FILE EMBASE
ANSWERS '56-68' FROM FILE WPIDS

=> d ibib ab hitrn 1-68

L228 ANSWER 1 OF 68 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 95353706 MEDLINE
DOCUMENT NUMBER: 95353706 PubMed ID: 7627566
TITLE: Anorexic action of a new potential neuropeptide Y antagonist [D-Tyr27,36, D-Thr32]-NPY (27-36) infused into the hypothalamus of the rat.
AUTHOR: Myers R D; Wooten M H; Ames C D; Nyce J W
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, East Carolina University, Greenville, NC 27858, USA.
SOURCE: BRAIN RESEARCH BULLETIN, (1995) 37 (3) 237-45.
Journal code: 7605818. ISSN: 0361-9230.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950921
Last Updated on STN: 19950921
Entered Medline: 19950907

AB Neuropeptide Y (NPY) produces a vigorous feeding response in several species when it is injected into hypothalamic structures involved in eating behavior. The purpose of this study was to determine whether a unique carboxy terminal fragment of NPY would alter the pattern of eating induced in the rat either by NPY injected into the hypothalamus or by a 24-h period of food deprivation. In this case, two L-tyrosine residues and one L-threonine residue of the NPY27-36 fragment were transformed to their D-conformation to produce [D-Tyr27,36,D-Thr32]-NPY (27-36), i.e., D-NPY27-36. Guide cannulae for microinjection were implanted stereotaxically just dorsal to the paraventricular nucleus (PVN) or ventromedial hypothalamus (VMH) of 24 adult male Sprague-Dawley rats. Following postoperative recovery, a microinjection of artificial CSF or 1.1 microgram or 3.3 micrograms of a peptide was made directly into the PVN or VMH as follows: native NPY; D-NPY27-36; or [L-Tyr27,36, L-Thr32]-NPY (27-36), i.e., L-NPY27-36. Food intakes were measured at intervals of 0.25, 0.5, 1.1, 2.0, 4.0, and 24 h. When D-NPY27-36 was microinjected at NPY reactive sites in the PVN or VMH of the rat 15 min before a similar microinjection of NPY, the intense eating response induced by the peptide was reduced significantly. Not only was the effect dose dependent, but D-NPY27-36 also augmented the latency to feed. A mixture of the two doses of NPY and D-NPY27-36 injected at the same hypothalamic loci did not attenuate the intake of food but tended to enhance the feeding response in the rats.(ABSTRACT TRUNCATED AT 250 WORDS)

L228 ANSWER 2 OF 68 MEDLINE
ACCESSION NUMBER: 2003017179 MEDLINE
DOCUMENT NUMBER: 22411424 PubMed ID: 12522988
TITLE: [Peptides are opening the door for novel treatments of obesity and loss of appetite].
Peptider oppnar for nya behandlingar av overvikt och aptitloshet.
AUTHOR: Broberger Christian; Hokfelt Tomas
CORPORATE SOURCE: Yale University, School of Medicine, Department of Neurobiology, New Haven, USA.. Christian.Broberger@yale.edu
SOURCE: LAKARTIDNINGEN, (2002 Dec 5) 99 (49) 4982-9. Ref: 151
Journal code: 0027707. ISSN: 0023-7205.
PUB. COUNTRY: Sweden

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Swedish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030114
Last Updated on STN: 20030306
Entered Medline: 20030305

AB A wide spectrum of diseases, as well as states of attenuated ability to heal and recover, can be traced to over- or underweight. Patients at the extremes of the energy balance spectrum are becoming more and more common. In order to provide adequate care for such patients an understanding of the mechanisms governing feeding behaviour is required. In the last decade, important advances have been made in this direction, as several factors mediating signals of hunger and satiety to and within the brain have been identified. These factors include hormonal signals (such as leptin and insulin) from the energy stores as well as neuronal influences (via the vagus nerve) from the digestive tract. The information encoded therein is routed to specific nuclei of the hypothalamus and brain stem, respectively, leading to activation of complex neuronal networks spanning the most rostral regions of the brain all the way to the effector neurones of the autonomic nervous system located in the spinal cord. Several recently characterized neuropeptides showing potent stimulation of appetite (neuropeptide Y, agouti gene-related peptide, orexin, **melanin-concentrating hormone**) and satiety (melanocortins, cholecystokinin, cocaine- and amphetamine-regulated transcript) have been localized to these pathways. These peptides, and the mechanisms through which they operate, offer promise for new therapeutic strategies in the treatment of obesity and anorexia.

L228 ANSWER 3 OF 68 MEDLINE
ACCESSION NUMBER: 2002434418 MEDLINE
DOCUMENT NUMBER: 22178860 PubMed ID: 12192103
TITLE: Intracerebroventricular leptin administration reduces food intake in pregnant and lactating mice.
AUTHOR: Mistry Anahita M; Romsos Dale R
CORPORATE SOURCE: Department of Food, Nutrition, and Exercise Sciences, Florida State University, Tallahassee, Florida 32306-1493, USA.
CONTRACT NUMBER: DK-15847 (NIDDK)
SOURCE: Exp Biol Med (Maywood), (2002 Sep) 227 (8) 616-9.
Journal code: 100973463. ISSN: 1535-3702.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020823
Last Updated on STN: 20020918
Entered Medline: 20020917

AB Leptin acts within the hypothalamus to diminish food intake. During pregnancy and lactation, both circulating leptin concentrations and food intake are elevated, suggesting an ineffectiveness of leptin to reduce food intake in these mice. Thus, this study tested the ability of intracerebroventricular (ICV) leptin administration to alter food intake during pregnancy and lactation. Mice during the first, second, and third trimesters of pregnancy, lactating mice on postpartum Day 7, and age-matched female mice were used. Plasma leptin concentrations averaged 2.9 +/- 0.3 ng/ml in control mice, increased steadily as pregnancy progressed (3.4 +/- 0.7, 29.8 +/- 4.5, and 40.5 +/- 0.7 ng/ml during the first, second, and third trimesters, respectively), and remained elevated on Day 7 postpartum (26.4 +/- 7.8 ng/ml). Mice were food deprived for 4

h, injected ICV with vehicle or leptin (1 micro g), and food intake was subsequently measured hourly for 3 hr, and after 24 hr. Vehicle-treated pregnant mice consumed marginally more food than cycling control mice, whereas nursing dams ate two to three times as much food as controls. As expected, ICV leptin administration reduced 24-hr food intake of control mice by 2 g, or approximately 50%. ICV-administered leptin was as effective in reducing food intake of pregnant and lactating mice as observed in control mice. Thus, the elevated circulating leptin concentrations observed in pregnant and nursing mice did not alter the ability of ICV-administered leptin to diminish food intake. High plasma concentrations of leptin-binding proteins observed during pregnancy, and probably during lactation, may limit the amount of endogenous leptin reaching the hypothalamus, and may consequently enable increases in food intake concomitant with elevated plasma leptin during these nutritionally demanding periods.

L228 ANSWER 4 OF 68 MEDLINE
ACCESSION NUMBER: 2002163846 MEDLINE
DOCUMENT NUMBER: 21893177 PubMed ID: 11896483
TITLE: Appetite suppression based on selective inhibition of NPY receptors.
AUTHOR: Chamorro S; Della-Zuana O; Fauchere J-L; Feletou M; Galizzi J-P; Levens N
CORPORATE SOURCE: Division of Metabolic Diseases, Institut de Recherches Servier, Suresnes, France.
SOURCE: INTERNATIONAL JOURNAL OF OBESITY AND RELATED METABOLIC DISORDERS, (2002 Mar) 26 (3) 281-98. Ref: 170
Journal code: 9313169. ISSN: 0307-0565.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020317
Last Updated on STN: 20020418
Entered Medline: 20020417

AB AIM: The aim of this review is to critically assess available evidence that blockade of the actions of NPY at one of the five NPY receptor subtypes represents an attractive new drug discovery target for the development of an appetite suppressant drug. RESULTS: Blockade of the central actions of NPY using anti-NPY antibodies, antisense oligodeoxynucleotides against NPY and NPY receptor antagonists results in a decrease in food intake in energy-deprived animals. These results appear to show that endogenous NPY plays a role in the control of appetite. The fact that NPY receptors exist as at least five different subtypes raises the possibility that the actions of endogenous NPY on food intake can be adequately dissociated from other effects of the peptide. Current drug discovery has produced a number of highly selective NPY receptor antagonists which have been used to establish the NPY Y(1) receptor subtype as the most critical in regulating short-term food intake. However, additional studies are now needed to more clearly define the relative contribution of NPY acting through the NPY Y2 and NPY Y5 receptors in the complex sequence of physiological and behavioral events that underlie the long-term control of appetite. CONCLUSIONS: Blockade of the NPY receptor may produce appetite-suppressing drugs. However, it is too early to state with certainty whether a single subtype selective drug used alone or a combination of NPY receptor selective antagonists used in combination will be necessary to adequately influence appetite regulation.

L228 ANSWER 5 OF 68 MEDLINE
ACCESSION NUMBER: 2001275854 MEDLINE

DOCUMENT NUMBER: 21263968 PubMed ID: 11371729
TITLE: Free-choice alcohol consumption in mice after application of the appetite regulating peptide leptin.
AUTHOR: Kiefer F; Jahn H; Wolf K; Kampf P; Knaudt K; Wiedemann K
CORPORATE SOURCE: Department of Psychiatry and Psychotherapy, University Hospital Hamburg, Hamburg, Germany.. kiefer@uke.uni-hamburg.de
SOURCE: ALCOHOLISM, CLINICAL AND EXPERIMENTAL RESEARCH, (2001 May) 25 (5) 787-9.
Journal code: 7707242. ISSN: 0145-6008.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809

AB BACKGROUND: Leptin has been shown to regulate food intake and energy expenditure. Very recently, associations of elevated leptin plasma levels during alcohol withdrawal with alcohol craving have been observed in humans. Therefore, we tested the hypothesis that the application of exogenous leptin modulates voluntary alcohol consumption in mice. METHODS: Sixteen mice (129/Sv x C57BL/6J) were habituated to ethanol consumption over a time period of 3 months. After a basal 2-week free-choice drinking phase, mice were separated into two groups (n = 8) according to weight and alcohol consumption. They received recombinant leptin (1 mg/kg) versus saline intraperitoneally daily for 10 days. After 4 days of free-choice consumption of ethanol (16% v/v) versus water, ethanol was withdrawn at day 4 and replaced at day 6 to test the occurrence of an alcohol deprivation effects. Fluid intake was evaluated by controlling the weight of the drinking tubes daily. RESULTS: Free-choice ethanol consumption after withdrawal was significantly elevated in mice after intraperitoneal injection of 1 mg/kg leptin (alcohol deprivation effect), but not during basal drinking. CONCLUSION: We suggest that leptin may enhance motivation for alcohol consumption in habituated mice after alcohol withdrawal.

L228 ANSWER 6 OF 68 MEDLINE
ACCESSION NUMBER: 2001270706 MEDLINE
DOCUMENT NUMBER: 21184998 PubMed ID: 11287112
TITLE: Does neuropeptide Y contribute to the anorectic action of amylin?.
AUTHOR: Morris M J; Nguyen T
CORPORATE SOURCE: Department of Pharmacology, The University of Melbourne, Melbourne, Australia.. mjmorris@unimelb.edu.au
SOURCE: PEPTIDES, (2001 Mar) 22 (3) 541-6.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB Neuropeptide Y (NPY) is a potent feeding stimulant acting at the level of the hypothalamus. Amylin, a peptide co-released with insulin from pancreatic beta cells, inhibits feeding following peripheral or central administration. However, the mechanism by which amylin exerts its anorectic effect is controversial. This study investigated the acute effect of amylin on food intake induced by NPY, and the effect of chronic amylin administration on food intake and body weight in male Sprague

Dawley rats previously implanted with intracerebroventricular (icv) cannulae. Rats received 1 nmol NPY, followed by amylin (0.05, 0.1, 0.5 nmol) or 2 microl saline. Increasing doses of amylin resulted in a dose-dependent inhibition of NPY-induced feeding by 31%, 74% and 99%, respectively ($P < 0.05$). To determine the chronic effects of i.c.v. amylin administration on feeding, rats received 0.5 nmol amylin or saline daily, 30 min before dark phase, over 6 days. Amylin significantly reduced food intake at 1, 4, 16 and 24 hours; after 6 days, amylin-treated rats showed a significant reduction in body weight, having lost 17.3 +/- 6.1 g, while control animals gained 7.7 +/- 5.1 g ($P < 0.05$). Brain NPY concentrations were not elevated, despite the reduced food intake, suggesting amylin may regulate NPY production or release. Thus, amylin potently inhibits NPY-induced feeding and attenuates normal 24 hour food intake, leading to weight loss.

L228 ANSWER 7 OF 68 MEDLINE
ACCESSION NUMBER: 2001683767 MEDLINE
DOCUMENT NUMBER: 21587037 PubMed ID: 11729633
TITLE: Potential molecular targets for anti-obesity drugs--after the discovery of leptin.
AUTHOR: Hidaka S; Ogawa Y; Nakao K
CORPORATE SOURCE: Department of Clinical Science and Medicine, Kyoto University Graduate School of Medicine, Sakyo-ku, Kyoto 606-8507, Japan.
SOURCE: NIPPON YAKURIGAKU ZASSHI. FOLIA PHARMACOLOGICA JAPONICA, (2001 Nov) 118 (5) 309-14. Ref: 34
Journal code: 0420550. ISSN: 0015-5691.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011204
Last Updated on STN: 20020216
Entered Medline: 20020215

AB The discovery of the adipose-derived hormone leptin has generated interest in the interaction between peripheral signals and brain targets involved in the regulation of feedings and energy balance. Potential anti-obesity drugs can be based on any intervention between the neuropeptide and its receptor that would alter the biological responses mediated by the neuronal network, in particular, food intake, metabolism and energy expenditure. Modulation of neurons in the arcuate nucleus by leptin results in reduced expression of neuropeptide Y and agouti-related protein, and increased expression of pro-opiomelanocortin (the precursor of a-melanocyte-stimulating hormone) and cocaine- and amphetamine-regulated transcript. Whether leptin finds its way into general usage as an anti-obesity drug, the use of modern methods to identify and target the components of leptin signaling pathway will form the basis for new pharmacological approaches to the treatment of obesity.

L228 ANSWER 8 OF 68 MEDLINE
ACCESSION NUMBER: 2001383668 MEDLINE
DOCUMENT NUMBER: 21238544 PubMed ID: 11340339
TITLE: Appetite-suppressing effects of urotensin I and corticotropin-releasing hormone in goldfish (Carassius auratus).
AUTHOR: Bernier N J; Peter R E
CORPORATE SOURCE: Department of Biological Sciences, University of Alberta, Edmonton, Alberta, Canada.
SOURCE: NEUROENDOCRINOLOGY, (2001 Apr) 73 (4) 248-60.
Journal code: 0035665. ISSN: 0028-3835.

PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB Fish urotensin I (UI), a member of the corticotropin-releasing hormone (CRH) family of peptides, is a potent inhibitor of food intake in mammals, yet the role of UI in the control of food intake in fish is not known. Therefore, to determine the acute effects of UI on appetite relative to those of CRH, goldfish were given intracerebroventricular (i.c.v.) injections of carp/goldfish UI and rat/human CRH (0.2-200 ng/g) and food intake was assessed for a 2-hour period after the injection. UI and CRH both suppressed food intake in a dose-related manner and UI (ED50 = 3.8 ng/g) was significantly more potent than CRH (ED50 = 43.1 ng/g). Pretreatment with the CRH receptor antagonist, alpha-helical CRH(9-41), reversed the reduction in food intake induced by i.c.v. UI and CRH. To assess whether endogenous UI and CRH modulate fish appetite, goldfish were given intraperitoneal implants of the glucocorticoid receptor antagonist, RU-486 (50 and 100 microg/g), or the cortisol synthesis inhibitor, metyrapone (100 and 200 microg/g), and food intake was monitored over the following 72 h. Fish treated with either RU-486 or metyrapone were characterized by a sustained and dose-dependent reduction in food intake. Pretreatment with i.c.v. implants of alpha-helical CRH(9-41) partially reversed the appetite-suppressing effects of RU-486 and metyrapone. In a parallel experiment, the effects of RU-486 (100 microg/g) and metyrapone (200 microg/g) intraperitoneal implants on brain UI and CRH gene expression were assessed. Relative to sham-implanted controls, fish treated with RU-486 or metyrapone had elevated UI mRNA levels in the hypothalamus and CRH mRNA levels in the telencephalon-preoptic brain region. Together, these results suggest that UI is a potent anorectic peptide in the brain of goldfish and that endogenous CRH-related peptides can play a physiological role in the control of fish appetite.

L228 ANSWER 9 OF 68 MEDLINE
ACCESSION NUMBER: 2001052393 MEDLINE
DOCUMENT NUMBER: 20502873 PubMed ID: 11044757
TITLE: Does drug therapy of obesity have a future?.
AUTHOR: Trakas K; Leiter L; Shear N H
SOURCE: CANADIAN JOURNAL OF CLINICAL PHARMACOLOGY, (2000 Autumn) 7 (3) 133-4. Ref: 31
Journal code: 9804162. ISSN: 1198-581X.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Editorial
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001213

L228 ANSWER 10 OF 68 MEDLINE
ACCESSION NUMBER: 2000389429 MEDLINE
DOCUMENT NUMBER: 20305787 PubMed ID: 10846432
TITLE: [Leptin and obesity: is the use of this hormone the solution to this illness?].
Leptina y obesidad: el uso de esta hormona es la solucion a esta enfermedad?.

AUTHOR: Gonzalez-Barranco J
SOURCE: REVISTA DE INVESTIGACION CLINICA, (2000 Mar-Apr) 52 (2) 113-4.
Journal code: 9421552. ISSN: 0034-8376.
PUB. COUNTRY: Mexico
DOCUMENT TYPE: Editorial
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000807

L228 ANSWER 11 OF 68 MEDLINE
ACCESSION NUMBER: 2000330710 MEDLINE
DOCUMENT NUMBER: 20330710 PubMed ID: 10869378
TITLE: Role of corticotropin-releasing factor (CRF) receptors in the anorexic syndrome induced by CRF.
AUTHOR: Pelleymounter M A; Joppa M; Carmouche M; Cullen M J; Brown B; Murphy B; Grigoriadis D E; Ling N; Foster A C
CORPORATE SOURCE: Department of Neuroscience, Pharmacology, and Peptide Chemistry, Neurocrine Biosciences, San Diego, CA 92121, USA.. MPelleymounter@neurocrine.com
CONTRACT NUMBER: 1R44NS35410-02 (NINDS)
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (2000 Jun) 293 (3) 799-806.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20021210
Entered Medline: 20000714

AB Genetic manipulations of corticotropin-releasing factor (CRF)(1) and CRF(2) receptors have resulted in data suggesting that the CRF(2) receptor could mediate the effects of CRF on appetite or satiety. We have attempted to obtain pharmacological evidence for this hypothesis by comparing the ability of a high-affinity peptide, mixed CRF antagonist [cyclo 30-33,f12,L18,21E30, A32,K33]sucker fish urotensin (12-41)NH(2) [cUTSN (12-41)] with a small-molecule CRF(1)-selective antagonist, NBI-27914, and a CRF(2)-selective peptide antagonist, antisauvagine-30, to attenuate the anorexic effects of CRF. We also monitored other behaviors that accompanied CRF-induced anorexia. CRF-induced anorexia was significantly correlated with a reduction in locomotor activity and an increase in freezing behavior and piloerection. cUTSN (12-41) and antisauvagine-30 significantly attenuated the effects of CRF (0.04 nmol) on food intake along with the behavioral syndrome that accompanied anorexia. In contrast, NBI-27914 did not attenuate either of the above-mentioned CRF-induced phenomena when given centrally at doses ranging from 0.13 to 10 nmol/2.5 microl or when given orally at 20 to 40 mg/kg. Although these data support the hypothesis that the CRF(2) receptor mediates the appetite suppression induced by CRF, they also suggest that the CRF(2) receptor could mediate the stress-like behaviors that accompany CRF-induced appetite suppression.

L228 ANSWER 12 OF 68 MEDLINE
ACCESSION NUMBER: 1999421237 MEDLINE
DOCUMENT NUMBER: 99421237 PubMed ID: 10493494
TITLE: Cancer anorexia-cachexia syndrome: are neuropeptides the key?.
AUTHOR: Inui A

CORPORATE SOURCE: Second Department of Internal Medicine, Kobe University School of Medicine, Japan.. inui@med.kobe-u.ac.jp
SOURCE: CANCER RESEARCH, (1999 Sep 15) 59 (18) 4493-501. Ref: 156
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 20000303
Entered Medline: 19991008

AB Progressive wasting is common in many types of cancer and is one of the most important factors leading to early death in cancer patients. Weight loss is a potent stimulus to food intake in normal humans and animals. The persistence of anorexia in cancer patients, therefore, implies a failure of this adaptive feeding response, although the weight loss in the patients differs from that found in simple starvation. Tremendous progress has been made in the last 5 years with regard to the regulation of feeding and body weight. It has been demonstrated that leptin, a hormone secreted by adipose tissue, is an integral component of the homeostatic loop of body weight regulation. Leptin acts to control food intake and energy expenditure via neuropeptidergic effector molecules within the hypothalamus. Complex interactions among the nervous, endocrine, and immune systems affect the loop and induce behavioral and metabolic responses. A number of cytokines, including tumor necrosis factor-alpha, interleukins 1 and 6, IFN-gamma, leukemia inhibitory factor, and ciliary neurotrophic factor have been proposed as mediators of the cachectic process. Cytokines may play a pivotal role in long-term inhibition of feeding by mimicking the hypothalamic effect of excessive negative feedback signaling from leptin. This could be done by persistent stimulation of anorexigenic neuropeptides such as corticotropin-releasing factor, as well as by inhibition of the neuropeptide Y orexigenic network that consists of opioid peptides and galanin, in addition to the newly identified **melanin-concentrating hormone,** orexin, and agouti-related peptide. Information is being gathered, although it is still insufficient, on such abnormalities in the hypothalamic neuropeptide circuitry in tumor-bearing animals that coincide with the development of anorexia and cachexia. Characterization of the feeding-associated gene products have revealed new biochemical pathways and molecular targets for pharmacological intervention that will likely lead to new treatments. Although therapeutic intervention using neuropeptide agonists/antagonists is now directed at obesity treatment, it may also have an effect on treating cancer anorexia-cachexia, especially when combined with other agents that have effects on muscle and protein breakdown.

L228 ANSWER 13 OF 68 MEDLINE
ACCESSION NUMBER: 1999325990 MEDLINE
DOCUMENT NUMBER: 99325990 PubMed ID: 10400403
TITLE: Current concepts in the pharmacological management of obesity.
AUTHOR: Carek P J; Dickerson L M
CORPORATE SOURCE: Medical University of South Carolina, Charleston 29425, USA.. carekpj@smtpgw2.musc.edu
SOURCE: DRUGS, (1999 Jun) 57 (6) 883-904. Ref: 125
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990921
Last Updated on STN: 20000303
Entered Medline: 19990903

AB The pharmacological management of obesity has gained increasing attention as new weight loss treatments are approved and a significant proportion of the public strives to lose weight. Obesity is associated with a high mortality rate, multiple chronic medical conditions, and carries an enormous financial burden. Obesity is a multifactorial condition, most often due to an imbalance in energy intake and expenditure. Despite the greater focus on management of obesity, weight loss remains a difficult goal to achieve. Obesity is a chronic medical condition that may require long term treatment, therefore the risks and benefits of all pharmacological agents must be carefully considered. Noradrenergic appetite suppressants (ie. phenyl-propanolamine, phentermine) result in weight loss but stimulatory effects limit their use. The serotonergic agents (fenfluramine, dexfenfluramine) were effective weight loss drugs, but were voluntarily withdrawn from the US market last year because of cardiovascular and pulmonary complications. The combination noradrenergic/serotonergic agent sibutramine is indicated for the management of obesity, particularly in the presence of other cardiovascular risk factors. Modest weight loss is achieved with sibutramine, although weight gain is significant after discontinuation. In addition, long term safety data are not yet available. The thermogenic combination of ephedrine plus caffeine is minimally effective, and adverse effects are usually transient. Other thermogenic agents, such as beta3-agonists, are still under investigation. Agents may alter digestion through lipase inhibition (orlistat) or fat substitution (olestra). Orlistat decreases systemic absorption of dietary fat, decreasing body weight and cholesterol. Olestra is a fat substitute that has been incorporated into snack foods. Olestra substitution for dietary fat has not been studied as a weight loss strategy, although olestra has no caloric value and may be beneficial. The use of orlistat and olestra may be limited by gastrointestinal adverse effects. Finally, the manipulation of leptin and neuropeptide Y are under investigation for the treatment of obesity. Pharmacological agents should be used as an aid to a structured diet and exercise regimen in the treatment of obesity. Weight loss agents may result in initial weight loss, but sustained weight loss is not always achieved even with continuation of treatment. The effect of weight loss obtained while using pharmacotherapeutic agents on morbidity and mortality has not been established. Therefore, diet and exercise should be the focus of any weight loss programme. There is a continued need for safe and effective pharmacotherapeutic agents for the treatment of obesity.

L228 ANSWER 14 OF 68 MEDLINE
ACCESSION NUMBER: 2000068337 MEDLINE
DOCUMENT NUMBER: 20068337 PubMed ID: 10604837
TITLE: Involvement of the histaminergic system in leptin-induced suppression of food intake.
AUTHOR: Morimoto T; Yamamoto Y; Mobarakeh J I; Yanai K; Watanabe T; Watanabe T; Yamatodani A
CORPORATE SOURCE: Department of Medical Physics, School of Allied Health Sciences, Faculty of Medicine, Osaka University, Suita, Japan.
SOURCE: PHYSIOLOGY AND BEHAVIOR, (1999 Nov) 67 (5) 679-83.
Journal code: 0151504. ISSN: 0031-9384.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001

ENTRY DATE: Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000112

AB The ob gene product leptin is secreted from white adipose tissue, and may regulate food intake by acting on the hypothalamus in the central nervous system. But the mechanism of this effect is still unclear. The central histaminergic system has been suggested to participate in the control of various physiological functions, particularly in feeding behavior, as it mediates anorectic signals like leptin. Thus, we hypothesized that the central histaminergic system is a target for leptin in its control of feeding. To prove this, we first examined the effect of i.p. administration of alpha-fluoromethylhistidine (FMH), a specific and irreversible inhibitor of histidine decarboxylase, on leptin-induced suppression of food intake in normal C57BL strain mice. Leptin treatment (1.3 mg/kg, i.p.) significantly reduced food intake by 60% of that of control at 6 h and by 84% at 24 h compared with control. When mice were injected with FMH (100 mg/kg, i.p.) before being given leptin, leptin-induced suppression of food intake was abolished and there was no significant difference compared with that of control. Additionally, we further examined the effects of leptin on food intake in mutant mice lacking histamine H, receptors (H1R-KO mice). Leptin injection significantly reduced food intake by 56% of that of control at 6 h and by 79% at 24 h in wild-type mice (WT mice), but not in H1R-KO mice. This finding suggests that leptin affects the feeding behavior through activation of the central histaminergic system via histamine H1 receptors.

L228 ANSWER 15 OF 68 MEDLINE
ACCESSION NUMBER: 1999385704 MEDLINE
DOCUMENT NUMBER: 99385704 PubMed ID: 10458522
TITLE: Corticotropin-releasing factor (CRF) induced anorexia is not influenced by a melanocortin 4 receptor blockage.
AUTHOR: Vergoni A V; Bertolini A; Wikberg J E; Schioth H B
CORPORATE SOURCE: Department of Biomedical Sciences, University of Modena, Italy.. helgis@bmc.uu.se
SOURCE: PEPTIDES, (1999) 20 (4) 509-13.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20020510
Entered Medline: 19991026

AB CRF and melanocortin (MSH/ACTH) peptides share a number of central effects including anorexia and grooming. The effects of CRF may be secondary, due to CRF's effects on melanocortin peptide release. We investigated if the newly discovered selective melanocortin 4 receptor antagonist HS014 could influence CRF induced anorexia and grooming. The data show that ICV administration of CRF (3 mg/rat), significantly reduced food intake, feeding time and feeding episodes whereas it increased grooming time and grooming episodes. HS014 (5 mg/rat), that previously has been shown to antagonize the anorectic effect and the excessive grooming induced by alpha-MSH, did however not influence any of the behavioral effects induced by CRF when the peptides were administered together. The data indicate that the anorectic and grooming effects of CRF are independent of pathways involving the MC4 receptors. These data suggest that the anorectic and grooming effect of CRF are not due to a secondary effect caused by increase in release of melanocortins acting on the central MC receptors.

L228 ANSWER 16 OF 68 MEDLINE
ACCESSION NUMBER: 1999007022 MEDLINE
DOCUMENT NUMBER: 99007022 PubMed ID: 9792536

TITLE: Functional interactions between **melanin-concentrating hormone**, neuropeptide Y, and anorectic neuropeptides in the rat hypothalamus.
AUTHOR: Tritos N A; Vicent D; Gillette J; Ludwig D S; Flier E S; Maratos-Flier E
CORPORATE SOURCE: Elliott P. Joslin Research Laboratory, Joslin Diabetes Center, Boston, Massachusetts 02215, USA.
CONTRACT NUMBER: I-K08-DK-02440 (NIDDK)
P30-DK-36836 (NIDDK)
SOURCE: DIABETES, (1998 Nov) 47 (11) 1687-92.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981110

AB A growing body of evidence indicates that a number of peptides expressed in the mammalian hypothalamus are involved in the regulation of food intake and energy balance. Among these, **melanin-concentrating hormone** (MCH) and neuropeptide Y (NPY) are potent appetite stimulants, whereas alpha-melanocyte-stimulating hormone (alpha-MSH), neurotensin, and glucagon-like peptide (GLP)-1(7-36) amide have appetite-suppressing properties. However, the functional interactions between pathways involving these neuropeptides remain incompletely understood. In the current study, we describe the functional interactions between orexigenic (appetite-stimulating: MCH and NPY) and anorectic (appetite-suppressing: alpha-MSH, neurotensin, and GLP-1) peptides after intracerebroventricular (i.c.v.) administration in the rat. The i.c.v. administration of GLP-1 completely prevents the orexigenic effects of both MCH and NPY. However, i.c.v. administration of alpha-MSH prevents only the orexigenic effect of MCH, as we have previously shown, but does not prevent the effect of NPY on food intake. Similarly, i.c.v. administration of neurotensin prevents only the orexigenic effect of MCH, but does not prevent the appetite-stimulating effect of NPY. Thus, our study suggests that the functional interactions between these neuropeptides are specific, although the underlying mechanisms are as yet unexplored.

L228 ANSWER 17 OF 68 MEDLINE
ACCESSION NUMBER: 1998294934 MEDLINE
DOCUMENT NUMBER: 98294934 PubMed ID: 9631473
TITLE: The role of CRF2 receptors in corticotropin-releasing factor- and urocortin-induced anorexia.
AUTHOR: Smagin G N; Howell L A; Ryan D H; De Souza E B; Harris R B
CORPORATE SOURCE: Pennington Biomedical Research Center, Lousiana State University, Baton Rouge 70808, USA.
SOURCE: NEUROREPORT, (1998 May 11) 9 (7) 1601-6.
Journal code: 9100935. ISSN: 0959-4965.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980903
Last Updated on STN: 19980903
Entered Medline: 19980824

AB The experiments presented in this study were designed to assess corticotropin-releasing factor (CRF) receptor subtype mediation of CRF- and urocortin (UCN)-induced decrease in food intake. Male Sprague-Dawley rats were treated with antisense and sense oligonucleotides (ON) to CRF2

receptor mRNAs for 36 h and then received an intracerebroventricular (i.c.v.) injection of CRF, UCN (3 micrograms) or saline. Antisense treatment significantly attenuated CRF- and UCN-induced suppression in food intake and HPA activation. Administration of CRF1 receptor antagonist did not affect the decrease in food intake or activation of the HPA axis induced by i.c.v. infusion of 3 micrograms CRF. The data suggest that down-regulation of CRF2 receptors selectively attenuates CRF- and UCN-induced anorexia and hypothalamo-pituitary-adrenocortical activation in rats.

L228 ANSWER 18 OF 68 MEDLINE
ACCESSION NUMBER: 1999126988 MEDLINE
DOCUMENT NUMBER: 99126988 PubMed ID: 9928027
TITLE: On the treatment of diabetes mellitus with **glucagon -like peptide-1**.
AUTHOR: Holst J J; Deacon C; Toft-Nielsen M B; Bjerre-Knudsen L
CORPORATE SOURCE: Department of Medical Physiology, Panum Institute, University of Copenhagen, Denmark.. holst@mfi.ku.dk
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1998 Dec 11) 865 336-43. Ref: 37
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990301
Last Updated on STN: 19990301
Entered Medline: 19990216

AB As a therapeutic principle, the insulinotropic peptide, GLP-1, of the secretin-glucagon family of peptides, has turned out to possess some remarkably attractive properties, including the capability of normalizing blood glucose concentrations in patients with non-insulin-dependent diabetes mellitus and promoting satiety and reducing food intake in healthy volunteers. Because of rapid and extensive metabolization, the peptide is not immediately clinically applicable and, as a therapeutic principle, GLP-1 is still in its infancy. Some possible avenues for circumventing these difficulties are the development of DPP-IV-resistant analogs, the inhibition of DPP-IV, enhancement of GLP-1 secretion, GLP delivery systems using continuous subcutaneous infusion or buccal tablets, GLP-1 absorption, and orally active, stable analogs. It seems likely that one or more of these approaches could result in a clinically useful development program.

L228 ANSWER 19 OF 68 MEDLINE
ACCESSION NUMBER: 1999126987 MEDLINE
DOCUMENT NUMBER: 99126987 PubMed ID: 9928026
TITLE: Is there appetite after GLP-1 and PACAP?.
AUTHOR: Christophe J
CORPORATE SOURCE: Department of General and Human Biochemistry, Universite Libre de Bruxelles, Brussels, Belgium.
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1998 Dec 11) 865 323-35. Ref: 88
Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902

ENTRY DATE: Entered STN: 19990301
Last Updated on STN: 19990301
Entered Medline: 19990216

AB Anitobesity drugs must increase the sensitivity of the hypothalamic satiety center towards leptin and antagonize the synthesis and action of NPY. The array of pharmacologic tools available is vast and presently ineffective. Among peptide analogs considered for evaluation [NPY-5 antagonists and CCK-A, bombesin, amylin and melanocyte-stimulating hormone-4 (or **melanin-concentrating hormone** ?) agonists], is there a place for GLP-1 and PACAP? GLP-1 receptors present in ARC, PVN, VMN, and SON are the target for both central and blood-borne GLP-1 in those hypothalamic neurons endowed with GLUT-2 and glucokinase. GLP-1, hypersecreted by L-cells after a meal, is a potent insulinotropic agent and, together with glucose, reduces food intake and induces c-fos in the ARC. PACAP is present in the ARC, PVN, and SCH, and its hypothalamic type I receptor elevates cAMP and inositol triphosphate in the PVN, where it may perhaps antagonize NPY-induced food intake and hyperinsulinemia. However, irrelevant neuroendocrine, autonomic, and circadian functions are also activated by this peptide, making it a less than ideal base on which to build an obesity treatment.

L228 ANSWER 20 OF 68 MEDLINE
ACCESSION NUMBER: 96365229 MEDLINE
DOCUMENT NUMBER: 96365229 PubMed ID: 8703220
TITLE: Appetite-suppressing effects of urocortin, a CRF-related neuropeptide.
AUTHOR: Spina M; Merlo-Pich E; Chan R K; Basso A M; Rivier J; Vale W; Koob G F
CORPORATE SOURCE: Department of Neuropharmacology, Scripps Research Institute, 10666 North Torrey Pines Road, La Jolla, CA 92037, USA.
CONTRACT NUMBER: 1 F05 TW05262 (FIC)
DK 26741 (NIDDK)
SOURCE: SCIENCE, (1996 Sep 13) 273 (5281) 1561-4.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961015
Last Updated on STN: 19980206
Entered Medline: 19960927

AB The neuropeptide corticotropin-releasing factor (CRF) is well known to act on the central nervous system in ways that mimic stress and result in decreases in exploration, increases in sympathetic activity, decreases in parasympathetic outflow, and decreases in appetitive behavior. Urocortin, a neuropeptide related to CRF, binds with high affinity to the CRF2 receptor, is more potent than CRF in suppressing appetite, but is less potent than CRF in producing anxiety-like effects and activation. Doses as low as 10 nanograms injected intracerebroventricularly were effective in decreasing food intake in food-deprived and free-feeding rats. These results suggest that urocortin may be an endogenous CRF-like factor in the brain responsible for the effects of stress on appetite.

L228 ANSWER 21 OF 68 MEDLINE
ACCESSION NUMBER: 94036223 MEDLINE
DOCUMENT NUMBER: 94036223 PubMed ID: 8221168
TITLE: Treatment with alpha-helical-CRF(9-41) prevents the anorectic effect of 17-beta-estradiol.
AUTHOR: Dagnault A; Ouerghi D; Richard D
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine, Laval University, Quebec City, Canada.

SOURCE: BRAIN RESEARCH BULLETIN, (1993) 32 (6) 689-92.
Journal code: 7605818. ISSN: 0361-9230.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931214

AB The role of corticotropin-releasing factor (CRF) in the anorexia induced by 17-beta-estradiol (E2) has been assessed in castrated female rats that were trained to eat their daily food ration in three separate meals. Each rat was implanted with a permanent guide cannula that was aimed at the right lateral ventricle of the brain. Seven days after the brain surgery each rat was also subcutaneously implanted with an osmotic minipump containing Buserelin, a potent GnRH agonist that induces reversible castration in rats. Eight rats were used in the study, and each of them underwent four experimental treatments that consisted of a) a subcutaneous (SC) injection of oil combined with an intracerebroventricular (ICV) infusion of saline, b) a SC injection of E2 combined with an ICV infusion of saline c) a SC injection of oil combined with an ICV infusion of alpha-helical CRF(9-41), and d) a SC injection of E2 combined with an ICV injection of alpha-helical CRF(9-41). Subcutaneous injections of E2 or oil were carried out the day before the ICV infusions of alpha-helical CRF(9-41) or saline. Intracerebroventricular infusions were performed 30 min before the meal for which the interaction effect of E2 and alpha-helical CRF(9-41) on food intake was determined. E2 and alpha-helical CRF(9-41) interacted on food intake; E2 brought about a 33% reduction in food intake in rats when infused with saline, whereas it was without effect when infused with alpha-helical-CRF(9-41)-treated rats. The present results provide evidence that CRF is involved in the anorectic effect of E2.

L228 ANSWER 22 OF 68 MEDLINE

ACCESSION NUMBER: 94147124 MEDLINE
DOCUMENT NUMBER: 94147124 PubMed ID: 8313139
TITLE: Evidence that neuropeptide Y and dopamine in the perifornical hypothalamus interact antagonistically in the control of food intake.
AUTHOR: Gillard E R; Dang D Q; Stanley B G
CORPORATE SOURCE: Department of Neuroscience, University of California, Riverside 92521.
CONTRACT NUMBER: NS 24268 (NINDS)
SOURCE: BRAIN RESEARCH, (1993 Nov 19) 628 (1-2) 128-36.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19970203
Entered Medline: 19940323

AB Mapping studies have revealed that the perifornical hypothalamus (PFH) is a primary locus for both the feeding-stimulatory effect of neuropeptide Y (NPY) and the anorectic effect of catecholamines (CAs), suggesting that NPY and CAs may interact antagonistically there. To investigate this, the CA-releasing agent amphetamine (AMPH) was injected through indwelling guide cannulas into the PFH of satiated adult male rats 5 min prior to injection of NPY (78 pmol/0.3 microliters) and food intake was measured 1, 2, and 4 h later. Amphetamine (50-200 nmol) dose-dependently reduced NPY feeding, usually eliminating it at the higher doses. The receptors

mediating this effect were investigated by sequential injection of various CA antagonists, AMPH, and NPY into the PFH. Neither the alpha- nor beta-adrenergic receptor antagonists phentolamine (100 nmol) or propranolol (200 nmol) significantly affected AMPH suppression of NPY feeding. In contrast, the dopamine receptor antagonist haloperidol (5 nmol) abolished AMPH suppression of NPY feeding, suggesting that dopamine (DA) mediates the AMPH effect. To examine this, epinephrine (EPI, 50-200 nmol) and DA (25-200 nmol) were tested for suppression of NPY-induced feeding. While EPI had no significant effect, DA at the maximally effective dose (50 nmol) reduced the NPY feeding response by 36% or more. These findings provide convergent evidence for antagonistic interactions between endogenous DA and NPY in the control of eating behavior.

L228 ANSWER 23 OF 68 MEDLINE
ACCESSION NUMBER: 93023553 MEDLINE
DOCUMENT NUMBER: 93023553 PubMed ID: 1383664
TITLE: Competitive antagonism of nitric oxide synthetase causes weight loss in mice.
AUTHOR: Morley J E; Flood J F
CORPORATE SOURCE: Geriatric Research Education and Clinical Center (GRECC), VA Medical Center, St. Louis, MO.
SOURCE: LIFE SCIENCES, (1992) 51 (16) 1285-9.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921026

AB These studies demonstrate that the competitive antagonist of nitric oxide synthesis, L-NG-nitro-arginine methyl ester (NO Arg ME), produces an L-arginine reversible decrease in food intake in mice. NO Arg ME also blocked the feeding effect of the potent orexigenic peptide, neuropeptide Y. NO Arg ME produced weight loss when administered over 5 days. The studies suggest that nitric oxide is a physiological modulator of food intake and that nitric oxide synthetase inhibitors may be useful in the management of obesity.

L228 ANSWER 24 OF 68 MEDLINE
ACCESSION NUMBER: 93073590 MEDLINE
DOCUMENT NUMBER: 93073590 PubMed ID: 1444178
TITLE: [Cholecystokinin, neurotensin and corticotropin-releasing factor, three important anorexic peptides].
Cholecystokinine, neurotensine et corticotropin-releasing factor, trois importants peptides anorexigenes.
AUTHOR: Beck B
CORPORATE SOURCE: INSERM U.308, Mecanismes de Regulation du Comportement Alimentaire, Nancy.
SOURCE: ANNALES D ENDOCRINOLOGIE, (1992) 53 (1) 44-56. Ref: 256
Journal code: 0116744. ISSN: 0003-4266.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921204

AB This paper updates the informations on the three most important

anorexigenic peptides: cholecystokinin, neurotensin and corticotropin-releasing factor. Their peripheral and/or central effects on food and water intakes as well as on dietary preferences are detailed. Their mechanisms of action and regulation are examined. This includes the interactions with classical neurotransmitters (norepinephrine, dopamine, etc...) as well as the description of the brain nuclei and neuronal networks involved. Finally, their variations in disturbed feeding behavior (hyperphagia, anorexia) in man or in animal models are reviewed.

L228 ANSWER 25 OF 68 MEDLINE
ACCESSION NUMBER: 91319907 MEDLINE
DOCUMENT NUMBER: 91319907 PubMed ID: 1862219
TITLE: Selective anorexigenic effects of corticotropin releasing hormone in the rhesus monkey.
AUTHOR: Glowa J R; Bacher J.D; Herkenham M; Gold P W
CORPORATE SOURCE: Clinical Neuroendocrinology Branch, NIMH, NIH, Bethesda, MD.
SOURCE: PROGRESS IN NEURO-PSYCHOPHARMACOLOGY AND BIOLOGICAL PSYCHIATRY, (1991) 15 (3) 379-91.
Journal code: 8211617. ISSN: 0278-5846.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910922
Last Updated on STN: 19970203
Entered Medline: 19910830

AB 1. Rhesus monkeys were equipped with a novel intracerebroventricular (i.c.v.) cannula system and trained to respond under operant schedules of food presentation or termination of stimuli associated with the delivery of shock (escape). 2. CRH decreased food-maintained behavior in a dose-related manner over the range of (0.3-10 micrograms/kg) but did not affect escape responding, demonstrating a selective effect on food-maintained responding. 3. This selective effect was related to the tendency for responding to stop after delivery of a food pellet when higher doses of CRH were given, consistent with the notion that a conditioned aversion to food was established in the presence of CRH. 4. This may suggest that in hyperaroused clinical states such as depression and anorexia nervosa, focus is shifted away from appetitive tasks as a result of increased levels of CRH.

L228 ANSWER 26 OF 68 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:5979 CAPLUS
DOCUMENT NUMBER: 138:49945
TITLE: Nitrogenous heterocyclic derivative, medicinal composition containing the same, medicinal use thereof, and intermediate therefor
INVENTOR(S): Nishimura, Toshihiro; Fujikura, Hideki; Fushimi, Nobuhiko; Tatani, Kazuya; Katsuno, Kenji; Isaji, Masayuki
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000712	A1	20030103	WO 2002-JP6000	20020617

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-187368 A 20010620
OTHER SOURCE(S): MARPAT 138:49945

AB A nitrogenous heterocyclic deriv. represented by the general formula (I), a pharmacol. acceptable salt thereof, or a prodrug of either. These have excellent human SGLT2 inhibitory activity and are useful as a preventive or remedy for diseases attributable to hyperglycemia such as diabetes. In the general formula [I; X1 and X3 each is nitrogen or CH; X2 is nitrogen or CR2; X4 is nitrogen or CR3 (provided that one or two of X1 to X4 are nitrogen); and R1, R2, and R3 are hydrogen, etc.].

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L228 ANSWER 27 OF 68 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:676030 CAPLUS
DOCUMENT NUMBER: 137:201524
TITLE: Preparation of glucopyranosyloxypyrazole derivatives as inhibitors of human SGLT2 (sodium-dependent glucose-transporter 2) and medicinal use thereof
INVENTOR(S): Fushimi, Nobuhiko; Fujikura, Hideki; Nishimura, Toshihiro; Katsuno, Kenji; Isaji, Masayuki
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068440	A1	20020906	WO 2002-JP1708	20020226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-53085 A 20010227
OTHER SOURCE(S): MARPAT 137:201524

AB 1-Phenyl-4-benzylpyrazol-3-yl glucopyranoside derivs. represented by the following general formula (I), pharmacol. acceptable salts thereof, or prodrugs thereof, [wherein R1, R2, R3 = H, halo; R4 = lower alkyl or haloalkyl; R5 = H, lower alkyl, alkoxy, alkylthio, haloalkyl, alkenyl, cycloalkyl, cycloalkoxy, or cycloalkylidenemethyl, halo, 5 or 6-membered arom. heterocyclyl contg. 1-4 heteroatoms selected from O, S, and N, (un)substituted Ph, HO-A (A = lower alkylene)] are prepd. These compds. I exhibit an excellent human SGLT2 activity inhibitory effect and thus being useful as preventives or remedies for diseases caused by hyperglycemia such as diabetes, diabetic complications, obesity, hyperinsulinism, glucose metab. disorder, hypercholesterolemia, hypertriglyceridemia, lipid metab. disorder, atherosclerosis, hypertension, ischemic heart failure, edema, hyperuricemia, and gout. Thus, to a soln. of 4-[(4-

methoxyphenyl)methyl]-5-methyl-1-phenyl-1,2-dihydro-3H-pyrazol-3-one 0.50, acetobromo-.alpha.-D-glucose 0.84, and benzyltri(n-butyl)ammonium chloride 0.53 g in 16 mL CH2Cl2 was added 4.3 mL 2 M aq. NaOH and stirred at room temp. for 1 h to give 0.38 g 4-[(4-methoxyphenyl)methyl]-5-methyl-1-phenyl-3-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyloxy)-1H-pyrazole which was treated with NaOMe in MeOH at room temp. for 1 h to give 0.32 g 4-[(4-methoxyphenyl)methyl]-5-methyl-1-phenyl-3-(.beta.-D-glucopyranosyloxy)-1H-pyrazole. 3-(.beta.-D-Glucopyranosyloxy)-4-[(4-isopropoxyphenyl)methyl]-5-methyl-1-phenyl-1H-pyrazole showed IC50 of .mu.g/mL of 200 nM for inhibiting the uptake of Me .alpha.-D-(U-14C)glucopyranoside in COS-7-cells overexpressing human SGLT2.

IT **169494-85-3, Leptin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(or analogs (appetite depressants), drugs contg.; prepn. of glucopyranosyloxypyrazole derivs. as inhibitors of human SGLT2 for prevention or treatment of diseases caused by hyperglycemia)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L228 ANSWER 28 OF 68 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:676029 CAPLUS
DOCUMENT NUMBER: 137:232854
TITLE: Preparation of glucopyranosyloxypyrazole derivatives as inhibitors of human SGLT2 (sodium-dependent glucose-transporter 2) activity
INVENTOR(S): Nishimura, Toshihiro; Fushimi, Nobuhiko; Fujikura, Hideki; Katsuno, Kenji; Komatsu, Yoshimitsu; Isaji, Masayuki
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068439	A1	20020906	WO 2002-JP1707	20020226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-51278 A 20010226
JP 2001-52903 A 20010227

OTHER SOURCE(S): MARPAT 137:232854

AB Benzylpyrazoylmethyl .beta.-D-glucopyranoside derivs. represented by the following general formula (I; wherein one of Q and T represents a group represented by the following general formula Q1 while the other represents lower alkyl or lower haloalkyl; R1 represents hydrogen, optionally substituted lower alkyl, lower alkenyl, cyclic lower alkyl, cyclic lower alkyl-lower alkyl, hydroxy-lower alkyl; R2 represents hydrogen, lower alkyl, lower alkoxy, lower alkylthio, halo-lower alkyl, halo, lower alkenyl, cyclic lower alkyl, cyclic lower alkoxy, cyclic lower alkylidenemethyl, (un)substituted Ph, 5 or 6-membered arom. heterocyclyl contg. 1-4 of same or different heteroatoms selected from O, S, and N, hydroxy-lower alkyl; provided that when R1 is hydrogen or lower alkyl, R2 is not H, lower alkyl, lower alkoxy, lower alkylthio, halo-lower alkyl, or

halo) or pharmacol. acceptable salts thereof or prodrugs thereof are prepd. These compds. exhibit an excellent human SGLT2 activity inhibitory effect and thus being useful as preventives or remedies for diseases caused by hyperglycemia such as diabetes, diabetic complications, obesity, hyperinsulinism (hyperinsulinemia), glucose metab. disorder, hypercholesterolemia, hypertriglyceridemia, lipid metab. disorder, atherosclerosis, hypertension, ischemic heart failure, edema, hyperuricemia, and gout. Thus, to a suspension of 0.026 g 5-methyl-4-{[4-(cyclopropylidenemethyl)phenyl]methyl}-1,2-dihydro-3H-pyrazol-3-one and acetobromo-.alpha.-D-glucose in THF was added 0.036 g Ag2CO3 and stirred at 60.degree. overnight under blocking light to give 0.010 g 5-methyl-4-{[4-(cyclopropylidenemethyl)phenyl]methyl}-3-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyloxy)-1H-pyrazole which (0.010 g) was treated with NaOMe in MeOH at room temp. for 30 min to give 0.0070 g 3-(.beta.-D-glucopyranosyloxy)-5-methyl-4-{[4-(cyclopropylidenemethyl)phenyl]methyl}-1H-pyrazole (II). II inhibited the uptake of Me .alpha.-D-(U-14C)glucopyranoside in COS-7 cell overexpressing human SGLT2 with IC50 of 15 nM.

IT **169494-85-3, Leptin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(or analogs (appetite depressants), drugs contg.; prepn. of glucopyranosyloxypyrazole derivs. as inhibitors of human SGLT2 for preventives or remedies for diseases caused by hyperglycemia)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L228 ANSWER 29 OF 68 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:637688 CAPLUS
DOCUMENT NUMBER: 137:185757
TITLE: Preparation of glucopyranosyloxybenzylbenzene derivatives as inhibitors of human SGLT2 (sodium-dependent glucose-transporter 2) activity and medicinal use thereof
INVENTOR(S): Fushimi, Nobuhiko; Tatani, Kazuya; Fujikura, Hideki; Nishimura, Toshihiro; Fujioka, Minoru; Nakabayashi, Takeshi; Isaji, Masayuki
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064606	A1	20020822	WO 2002-JP1178	20020213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-37729 A 20010214
OTHER SOURCE(S): MARPAT 137:185757

AB 2-Benzylphenyl .beta.-D-glucopyranoside derivs. represented by the following general formula (I) and pharmacol. acceptable salts thereof [wherein P = H, a group constituting a prodrug; R1 = H, NH2, mono- or di(lower alkyl)amino, carbamoyl, lower alkyl, lower alkoxy, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy, carbamoyl-lower alkyl,

carboxy-lower alkoxy, P1-O-A1- (wherein P1 = H, a group constituting a prodrug; A1 = a single bond, lower alkylene or alkyleneoxy); R2 = H, lower alkyl; R3 = lower alkyl, lower alkoxy, lower alkylthio, lower alkenyloxy, aralkyloxy, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy, lower alkoxy-lower alkylthio, CO2H, lower alkoxycarbonyl, cyano, aralkyloxy-lower alkyl, cyano-lower alkyl, CONH2, carbamoyl-lower alkyl, NH2, mono- or di(lower alkyl)amino, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkoxy, P2-O-A2- (wherein P2 = H, a group constituting a prodrug; A2 - lower alkylene, lower alkyleneoxy, lower alkylenethio, lower alkenylene); some provisos are given] are prepd. These compds. are useful as preventives or remedies for diseases caused by hyperglycemia such as diabetes, diabetes complications, obesity, hyperinsulinism, glucose metab., hyperlipidemia, hypercholesteremia, hypertriglycemia, abnormal lipid metab., atherosclerosis, hypertension, ischemic heart failure, edema, hyperuricemia, and gout because of having an improved oral absorbability and exerting an excellent human SGLT2 activity inhibitory effect (in vivo). Thus, 0.037 mL Et chloroformate was added to a soln. of 0.075 g 2-(4-ethylbenzyl)-5-hydroxymethylphenyl .beta.-D-glucopyranoside in 2 mL 2,4,6-trimethylpyridine and stirred at room temp. for 17 h to give 0.020 g 2-(4-ethylbenzyl)-5-hydroxymethylphenyl 6-O-ethoxycarbonyl-.beta.-D-glucopyranoside (II). Oral bioavailability (serum concn.) of II was 43% of that of i.v. administration in SD rats. II increased the excretion of glucose in urine from 7.0 mg/24 h/200 g body wt. at 1 mg/kg body wt. to 195 mg/24 h/200 g body wt. at 10 mg/kg body wt. when fed p.o. to SD rats.

IT **169494-85-3, Leptin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(or analogs thereof (appetite depressants), drugs contg.; prepn. of glucopyranosyloxybenzylbenzene derivs. as inhibitors of human SGLT2 activity for prevention or treatment of diseases caused by hyperglycemia)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L228 ANSWER 30 OF 68 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:521754 CAPLUS
DOCUMENT NUMBER: 137:93946
TITLE: Preparation of glucopyranosyloxypyrazole derivatives as inhibitors of human SGLT2 (sodium-dependent glucose-transporter 2) activity and use thereof in medicines
INVENTOR(S): Fujikura, Hideki; Fushimi, Nobuhiko; Nishimura, Toshihiro; Nakabayashi, Takeshi; Isaji, Masayuki
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053573	A1	20020711	WO 2001-JP11348	20011225

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2000-403534 A 20001228

OTHER SOURCE(S): MARPAT 137:93946

AB Glucopyranosyloxypyrazole derivs. represented by the general formula (I) or pharmacol. acceptable salts thereof [wherein R is hydrogen, lower alkyl, or a prodrug-constituting group; one of Q and T is a group of the general formula Q (wherein P is hydrogen or a prodrug-constituting group), and the other is lower alkyl or halogenated lower alkyl; and R2 is hydrogen, lower alkyl, lower alkoxy, lower alkylthio, halogenated lower alkyl, or halogeno, with the proviso that when R is hydrogen or lower alkyl, P is not hydrogen] are prepd. These compds. exhibit human SGLT2 inhibiting activity and are improved in peroral absorbability and useful as preventive or therapeutic drugs for diseases due to hyperglycemia, e.g., diabetes, complications of diabetes, and obesity. Other diseases caused by hyperglycemia include hyperinsulinism, abnormal glucose metab., hyperlipidemia, hypercholesteremia, hypertriglycemia, abnormal lipid metab., atherosclerosis, hypertension, ischemic heart failure, edema, hyperuricemia, and gout. Thus, to soln. of 3-(.beta.-D-glucopyranosyloxy)-4-[(4-isopropoxyphenyl)methyl]-1-isopropyl-5-methylpyrazole in 2,4,6-trimethylpyridine was added Et chloroformate and stirred at room temp. overnight to give 4-[(4-isopropoxyphenyl)methyl]-3-(6-O-methoxycarbonyl-.beta.-D-glucopyranosyloxy)-1-isopropyl-5-methylpyrazole (II). Oral bioavailability of II was 27% of that of i.v. administration in SD rats and II increased the urinary secretion of glucose from 1.7 mg/24 h/200 g body wt. at 1 mg/kg to 167.3 mg/24 h/20 g body wt. at 10 mg/kg.

IT **169494-85-3, Leptin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(or analogs or receptor agonists (appetite depressant), drugs contg.; prepn. of glucopyranosyloxypyrazole derivs. as inhibitors of human SGLT2 activity for prevention or treatment of diseases caused by hyperglycemia)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L228 ANSWER 31 OF 68 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:617765 CAPLUS
DOCUMENT NUMBER: 135:180248
TITLE: Weight loss induced by reduction in neuropeptide **Y** level
INVENTOR(S): Loftus, Thomas M.; Townsend, Craig A.; Ronnett, Gabriele; Lane, M. Daniel; Kuhajda, Francis P.
PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine, USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060174	A2	20010823	WO 2001-US5316	20010216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001038515	A5	20010827	AU 2001-38515	20010216
EP 1259121	A2	20021127	EP 2001-910959	20010216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 2000-182901P P 20000216
US 2000-208560P P 20000602
WO 2001-US5316 W 20010216

AB This invention provides a method for inducing wt. loss in an animal by administering to the animal a compd. which reduces the expression and/or secretion of neuropeptide Y (NPY). The effect may be accomplished directly, indirectly or humorally. Preferably, administration of this compd. has the effect of increasing malonyl CoA levels in the animal. Compds. administered according to this invention may be inhibitors of fatty acid synthase (FAS), including substituted .alpha.-methylene-.beta.-carboxy-.gamma.-butyrolactones, or inhibitors of malonyl CoA decarboxylase (MCD). Preferably, the compd. is administered in an amt. sufficient to reduce the amt. and/or duration of expression and/or secretion of NPY to levels at or below those obsd. for lean animals. In another preferred embodiment, the administration will reduce expression and/or secretion to levels obsd. for fed or satiated animals; more preferably, administration will reduce the level of NPY below that of fed animals. In a particular embodiment, this invention provides a method for inducing wt. loss in an animal by administering a compd. which inhibits feeding behavior in the animal. The method is particularly useful for inducing wt. loss in animals deficient in expression of the hormone leptin or animals resistant to the action of leptin.

IT **169494-85-3, Leptin**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(wt. loss induced by redn. in neuropeptide Y level)

L228 ANSWER 32 OF 68 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:709687 CAPLUS
DOCUMENT NUMBER: 135:272869
TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 **diabetes**
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
EP 1136071	A3	20030326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319
CA 2341344	AA	20010922	CA 2001-2341344	20010320
US 2003004162	A1	20030102	US 2001-813335	20010320
NZ 510677	A	20021025	NZ 2001-510677	20010321

PRIORITY APPLN. INFO.: US 2000-191381P P 20000322
OTHER SOURCE(S): MARPAT 135:272869

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH2, CH-alkyl when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6- or 7-NO2, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R2 = H; R3 = H, alkyl; R4 = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R5 = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R7 = H, F, alkyl; or R5 and R7 can be taken together to be oxo; R6 = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R9 = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and

derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **169494-85-3, Leptin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical in combination with; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L228 ANSWER 33 OF 68 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:293388 CAPLUS
DOCUMENT NUMBER: 129:599
TITLE: Combination therapy for the treatment of **diabetes** and obesity
INVENTOR(S): Smith, Roy G.; Cascieri, Margaret A.; MacIntyre, Euan; MacNeil, Douglas J.; Menke, John G.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Smith, Roy G.; Cascieri, Margaret A.; Macintyre, Euan; Macneil, Douglas J.; Menke, John G.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818481	A1	19980507	WO 1997-US19880	19971030
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851606	A1	19980522	AU 1998-51606	19971030
AU 723879	B2	20000907		
US 5908830	A	19990601	US 1997-961749	19971030
EP 969852	A1	20000112	EP 1997-946442	19971030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002516605	T2	20020604	JP 1998-520803	19971030

PRIORITY APPLN. INFO.:
US 1996-29233P P 19961031
GB 1997-11042 A 19970530
WO 1997-US19880 W 19971030

AB The combination of a metabolic rate-modifying agent (e.g., a .beta.3 adrenergic receptor agonist) and a feeding behavior modifying agent (e.g., a NPY5 antagonist) is useful in the treatment of obesity and diabetes, either as compds., pharmaceutically acceptable salts, or pharmaceutical compn. ingredients. Methods of treating obesity and diabetes are also described.

IT **169494-85-3, Leptin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(combination therapy for the treatment of diabetes and obesity)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L228 ANSWER 34 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003029126 EMBASE
TITLE: Targeted disruption of H3 receptors results in changes in brain histamine tone leading to an obese phenotype.
AUTHOR: Takahashi K.; Suwa H.; Ishikawa T.; Kotani H.
CORPORATE SOURCE: H. Kotani, Banyu Tsukuba Research Institute, Okubu 3, Tsukuba, Ibaraki 300-2611, Japan. kotanihh@banyu.co.jp
SOURCE: Journal of Clinical Investigation, (2002) 110/12 (1791-1799).
Refs: 46
ISSN: 0021-9738 CODEN: JCINAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Histamine is an aminergic neurotransmitter that is localized in the CNS and in peripheral tissues. To date, four histamine receptors have been identified, and the H3 receptor, which was recently cloned, is predominantly expressed in the CNS. The peripheral functions of histamine have been investigated intensively using available molecular and pharmacological tools, and the molecular identification of the H3 receptor opens up new possibilities for investigating the role of histamine in central tissues. To understand the biological function of the histamine presynaptic autoreceptor H3, we inactivated the receptor through homologous recombination. H3-/- mice manifest mild obese phenotypes that are characterized by increases in body weight, food intake, and adiposity and by reductions in energy expenditure. Consistent with these observations, homozygous null mice have insulin and leptin resistance, increased levels of plasma leptin and insulin, and decreased levels of histamine in the hypothalamic/thalamic region of their brains coupled with increased histamine turnover. The expression of UCP1 in brown adipose tissue and of UCP3 in brown adipose tissue, white adipose tissue, and skeletal muscle is decreased in H3-/- mutants, and the anorexigenic activity of thioperamide is not observed. These results suggest that neuronal histamine is a mediator of body-weight homeostasis and that neuronal histamine functions through H3 receptors in mice.

L228 ANSWER 35 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002380375 EMBASE
TITLE: Acute and chronic administration of melanin-concentrating hormone enhances food intake and body weight in Wistar and Sprague-Dawley rats.
AUTHOR: Della-Zuana O.; Presse F.; Ortola C.; Duhault J.; Nahon J.L.; Levens N.
CORPORATE SOURCE: N. Levens, Division of Metabolic Diseases, Institut de Recherches Servier, 92150 Suresnes, France. nigel.levens@fr.netgrs.com
SOURCE: International Journal of Obesity, (2002) 26/10 (1289-1295).
Refs: 22
ISSN: 0307-0565 CODEN: IJOBDP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB AIM: Although melanin-concentrating hormone (MCH) is believed to be an important regulator of feeding behavior, both its acute and chronic effects on food intake as well as its interaction with other brain

peptides involved in the control of appetite remain unclear. Therefore, the acute effects of MCH on food intake and the chronic effect of MCH on food intake and the gene expression of various hypothalamic peptides involved in the control of appetite were studied in rats. METHODS AND RESULTS: Either the acute or the continuous intraventricular infusion of MCH for 12 days stimulated feeding in both Wistar or Sprague-Dawley rats. Removal of the hypothalamus at the end of the chronic infusion studies allowed measurement of the expression of mRNAs encoding for MCH, neuropeptide Y (NPY), orexin, agouti gene-related peptide, cocaine and amphetamine-related transcript and neurotensin-neuropeptides involved in the control of appetite. Chronic intraventricular infusion of MCH activated only NPY mRNA synthesis in Sprague-Dawley rats. The increase in food intake in response to MCH in Sprague-Dawley rats did not appear to be due to the release of NPY since combination studies demonstrated consistently additive effects of the two peptides on food intake at maximum or near maximum doses. CONCLUSIONS: These results strongly suggest that MCH is an orexigenic peptide involved in the control of both short- and long term food intake in satiated rats and further indicate that the MCH pathway is a possible target for the control of food intake and obesity.

L228 ANSWER 36 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002449009 EMBASE
TITLE: New pharmacological tools for obesity.
AUTHOR: Nisoli E.; Carruba M.O.
CORPORATE SOURCE: Prof. E. Nisoli, Center for Study and Res. on Obesity, University of Milan, Department of Preclinical Science,, Via G.B. Grassi 74, 20157 Milano, Italy. enzo.nisoli@unimi.it
SOURCE: Journal of Endocrinological Investigation, (2002) 25/10 (905-914).
Refs: 84
ISSN: 0391-4097 CODEN: JEIND7
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
005 General Pathology and Pathological Anatomy
038 Adverse Reactions Titles
036 Health Policy, Economics and Management
003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Obesity is a multi-factorial, chronic disorder that has reached epidemic proportions in most industrialized countries and is threatening to become a global epidemic. Obese patients are at a higher risk from coronary artery disease, hypertension, hyperlipidemia, diabetes mellitus, certain cancers, cerebrovascular accidents, osteoarthritis, restrictive pulmonary disease, and sleep apnea. Obesity is a particularly challenging clinical condition to treat, because of its complex pathophysiological basis. Indeed, body weight represents the integration of many biological and environmental components. Efforts to develop innovative anti-obesity drugs have been recently intensified. In broad terms, researchers use different distinct strategies: first, to reduce energy intake; second, to increase energy expenditure; third, to alter the partitioning of nutrients between fat and lean tissue. In the present review we concentrate on the first of these strategies, by underlining the new pharmacological tools which are presently studied. .COPYRGT.2002, Editrice Kurtis.

L228 ANSWER 37 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002389065 EMBASE
TITLE: [Innovative neuropeptide antagonist - Antidepressant, anxiolytic and at the same time appetite stimulating?]. INNOVATIVER NEUROPEPTID-ANTAGONIST - ANTIDEPRESSIV, ANGSTLOSEND UND GLEICHZEITIG APPETITZUGELND?.
AUTHOR: Bruhn C.
SOURCE: Deutsche Apotheker Zeitung, (17 Oct 2002) 142/42 (41). ISSN: 0011-9857 CODEN: DAZEA2
COUNTRY: Germany
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: German

L228 ANSWER 38 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001418628 EMBASE
TITLE: Recent insights into body weight control: From physiology to pathology.
AUTHOR: Krysiak R.; Okopien B.; Belowski D.; Madej A.; Herman Z.S.
CORPORATE SOURCE: Dr. R. Krysiak, Department of Clinical Pharmacology, Medical University of Silesia, Medykow 18, PL 40-752 Katowice, Poland
SOURCE: Journal of Peptide Science, (2001) 7/11 (571-578). Refs: 61
ISSN: 1075-2617 CODEN: JPSIEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Over the past several years, new modulators of feeding and body weight have been discovered, and our knowledge of the mechanisms and neurohumoral interactions between anorexigenic and orexigenic compounds has increased dramatically. This review aims to summarize the present knowledge of the role of leptin and several hypothalamic neuropeptides, such as neuropeptide Y (NPY), corticotropin-releasing hormone (CRH) and melanocortins, in the regulation of appetite and body weight. It also presents the progress made in the design of interactions between leptin and hypothalamic peptides in the regulation of feeding. The role of these compounds in the pathogenesis of obesity in animals and humans, and their potential usefulness in the treatment of this disorder, are discussed. Copyright .COPYRGT. 2001 European Peptide Society and John Wiley & Sons, Ltd.

L228 ANSWER 39 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001421953 EMBASE
TITLE: Pharmacology of appetite suppression: Implication for the treatment of obesity.
AUTHOR: Halford J.C.G.
CORPORATE SOURCE: J.C.G. Halford, Kissileff Lab. Stud. of Hum. Ingest., Department of Psychology, University of Liverpool, Bedford Street South, Liverpool L68 7ZA, United Kingdom. j.c.g.halford@liverpool.ac.uk
SOURCE: Current Drug Targets, (2001) 2/4 (353-370). Refs: 256
ISSN: 1389-4501 CODEN: CDTUAU
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Given the current global epidemic of obesity there is a demand for new anti-obesity drugs to overcome the problem. Many pharmacological agents reduce food intake and significantly decrease body mass when administered to animals but affect feeding behaviour in a profoundly different way indicating the variety of biological mechanisms by which such agents act (appetite verses non-appetite). More limited clinical data demonstrates that some of the same drugs produce decreases in food intake and weight loss in humans. A few of these drugs do so by modifying the functioning of the appetite system as measured by subjective changes in feelings of hunger and fullness (indices of satiety). These drugs that modify the daily flux of appetite could be considered as 'appetite suppressants' with clinical potential as anti-obesity agents. Drugs that can be considered suitable candidates for appetite suppressants are agents that enhance peripherally satiety peptide systems (such as CCK, Bombesin/GRP, Enterostatin and GLP-1), alter the CNS levels of various hypothalamic neuropeptides (NPY, Galanin, Orexin, CART and Melanocortins) or monoamine neurotransmitters (such as serotonin, nor-adrenaline and possibly dopamine). Recently, the hormone leptin has become regarded as a key hormonal signal linking adipose tissue status with a number of key central nervous system circuits (NPY, CART, CRF, Melanocortins and possibly Orexins). This tonic system may also provide drug targets for the control of appetite. Any changes induced by a potential appetite suppressant should be considered in terms of the (i) psychological experience and behavioural expression of appetite, (ii) metabolism and peripheral physiology, and (iii) functioning of CNS neural pathways. In humans, such modulation of appetite will involve changes in total caloric consumption, subjective changes in feelings of hunger and fullness, preferences for specific food items, and general macronutrient preferences. These may be expressed behaviourally as changes in meal patterns, snacking behaviour and food choice. Within the next 20 years it is certain that clinicians will have a new range of anti-obesity compounds available to choose from. Such novel compounds may act on a single component of the appetite system or target a combination of these components detailed in this review. Such compounds used in combination with life style changes and dietary intervention may be critical in dealing with the rising world epidemic of obesity.

L228 ANSWER 40 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000241016 EMBASE
TITLE: Melanin-concentrating hormone regulates leptin synthesis and secrection in rat adipocytes.
AUTHOR: Bradley R.L.; Kokkotou E.G.; Maratos-Flier E.; Cheatham B.
CORPORATE SOURCE: Dr. B. Cheatham, Joslin Diabetes Center, One Joslin Pl., Boston, MA 02215, United States.
bentley.cheatham@joslin.harvard.edu
SOURCE: Diabetes, (2000) 49/7 (1073-1077).
Refs: 35
ISSN: 0012-1797 CODEN: DIAEAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Obesity is a common problem in Western society and is associated with significant morbidity and mortality. Energy homeostasis is regulated by a

complex system involving both peripheral signals such as leptin and a number of orexigenic and anorectic neuropeptides. Obesity can result from dysregulation of the peripheral and/or central signals. Melanin-concentrating hormone (MCH) is a hypothalamic peptide that is important in the regulation of feeding behavior, primarily via uncharacterized signaling pathways in the central nervous system. Leptin, expressed in adipose tissue, mediates some of its actions through several hypothalamic neuropeptides, notably agouti- related peptide, proopiomelanocortin, and neuropeptide Y. Expression of leptin is regulated by dietary status, insulin, and glucocorticoids. Furthermore, certain neuropeptides may act on adipocytes. However, the potential effect of MCH has not been investigated. We report that MCH stimulates leptin mRNA expression and leptin secretion. MCH stimulated a 2- fold increase in leptin secretion by isolated rat adipocytes after 4 h of treatment. This increase in secreted leptin was preceded by a rapid and transient increase in ob mRNA levels; MCH stimulated a 2.5-fold increase in ob mRNA within 1 h of treatment, followed by a decline to basal levels within 4 h. In addition, we demonstrate that the MCH receptor SLC-1 is expressed in adipocytes, suggesting that fat cells may be targets of MCH or an MCH-like peptide under physiological conditions. Finally, using a radioimmunoassay, MCH/MCH-like peptide was detected in rat plasma. This study establishes a novel in vitro mammalian system for examining MCH signaling pathways.

L228 ANSWER 41 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000322596 EMBASE
TITLE: Apetite regulation: New opportunities for weight control.
AUTHOR: Morgan D.
CORPORATE SOURCE: Dr. D. Morgan, Department of Metabolic Medicine, Imperial Collége Sch. of Medicine, Hammersmith Campus, Du-Cane Road, London W12 ONN, United Kingdom. d.morgan@ic.ac.uk
SOURCE: Proceedings of the Nutrition Society, (2000) 59/3 (431). ISSN: 0029-6651 CODEN: PNUSA4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English

L228 ANSWER 42 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000180096 EMBASE
TITLE: Cocaine- and amphetamine-regulated transcript, glucagon-like peptide-1 and corticotrophin releasing factor inhibit feeding via agouti-related protein independent pathways in the rat.
AUTHOR: Edwards C.M.B.; Abbott C.R.; Sunter D.; Kim M.-S.; Dakin C.L.; Murphy K.G.; Abusnana S.; Taheri S.; Rossi M.; Bloom S.R.
CORPORATE SOURCE: S.R. Bloom, ICSM Endocrine Unit, Hammersmith Hospital, London W12 ONN, United Kingdom. s.bloom@ic.ac.uk
SOURCE: Brain Research, (2 Jun 2000) 866/1-2 (128-134). Refs: 28
ISSN: 0006-8993 CODEN: BRREAP
PUBLISHER IDENT.: S 0006-8993(00)02257-5
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
003 Endocrinology
030 Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The melanocortin-4 receptor (MC4-R) appears to be an important downstream mediator of the action of leptin. We examined to what extent the anorectic effects of cocaine- and amphetamine-regulated transcript (CART), glucagon-like peptide-1 (GLP-1) and corticotrophin releasing factor (CRF) might be mediated via MC4-R. .alpha.-Melanocyte stimulating hormone (.alpha.-MSH), the MC4-R agonist, administered intracerebroventricularly (ICV) at a dose of 1 nmol reduced food intake by approximately half. Agouti-related protein (Agrp) (83-132), a biologically active fragment of the endogenous MC4-R antagonist, administered ICV at a dose of 1 nmol completely blocked the anorectic effect of 1 nmol .alpha.-MSH. CART (55-102) (0.2 nmol), GLP-1 (3 nmol) and CRF (0.3 nmol) produced a reduction in feeding of approximately the same magnitude as 1 nmol .alpha.-MSH. Agrp (83-132) (1 nmol) administered ICV did not block the anorectic effects of CART (55-102) (1 h food intake, 0.2 nmol CART (55-102), 2.7.+-.0.8 g vs. CART (55-102)+Agrp (83-132), 2.6.+-.0.6 g, P=0.87; saline control 5.4.+-.0.3 g, P<0.001 vs. both groups). Agrp (83-132) also did not block the anorectic effects of GLP-1 or CRF (1 h food intake, 0.3 nmol CRF, 0.7.+-.0.3 g vs. CRF+Agrp (83-132), 0.7.+-.0.3 g, P=0.91; 3 nmol GLP-1, 1.9.+-.0.4 g vs. GLP-1+Agrp (83-132), 1.1.+-.0.5 g, P=0.23; saline control 5.0.+-.0.6 g, P<0.001 vs. all four groups). Thus, as previous data suggests, GLP-1 and CRF do not appear to reduce food intake predominantly via MC4-R, we here demonstrate for the first time that CART, in addition to GLP-1 and CRF primarily acts via Agrp independent pathways. Copyright (C) 2000 Elsevier Science B.V.

L228 ANSWER 43 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000178801 EMBASE
TITLE: Pharmacology of appetite suppression.
AUTHOR: Halford J.C.G.; Blundell J.E.
CORPORATE SOURCE: Dr. J.C.G. Halford, Department of Psychology, University of Liverpool, Liverpool L69 3BX, United Kingdom
SOURCE: Progress in Drug Research, (2000) 54/- (25-58).
Refs: 151
ISSN: 0071-786X CODEN: FAZMAE
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Despite a rising worldwide epidemic of obesity there is currently only a very small number of anti-obesity drugs available to manage the problem. Large numbers of differing pharmacological agents reliably produce a reduction in food intake when administered acutely to animals, and when administered chronically they result in a significant decrease in body mass. Behavioural analysis of drug-induced anorexia in animals demonstrates that various compounds profoundly effect feeding behaviour in differing ways. This indicates the variety of mechanisms by which pharmacological agents can induce changes in food intake, body weight and eventually body composition. Some of the same drugs produce decreases in food intake and weight loss in humans. Some of these drugs do so by modifying the functioning of the appetite system as measured by subjective changes in feelings of hunger and fullness (indices of satiety). Such drugs can be considered as 'appetite suppressants' with clinical potential as anti-obesity agents. Other drugs induce changes in food intake and body weight through various physiological mechanisms inducing feelings of nausea or even by side effect related malaise. Of the drugs considered suitable candidates for appetite suppressants are agents which act via peripherally satiety peptide systems (such as CCK, Bombesin/GRP Enterostatin and GLP-1), or alter the CNS levels of various hypothalamic neuropeptides (NPY, Galanin, Orexin and Melanocortins) or levels of the

key CNS appetite monoamine neurotransmitters such as serotonin (5-HT) and noradrenaline (NA). Recently, the hormone leptin has been regarded as a hormonal signal linking adipose tissue status with a number of key central nervous system circuits. The peptide itself stimulates leptin receptors and it links with POMC and MC-4 receptors. These receptors may also provide drug targets for the control of appetite. Any changes induced by a potential appetite suppressant should be considered in terms of the (i) psychological experience and behavioural expression of appetite, (ii) metabolism and peripheral physiology, and (iii) functioning of CNS neural pathways. In humans, modulation of appetite may involve changes in total caloric consumption, subjective changes in feelings of hunger and fullness, preferences for specific food items, and general macronutrient preferences. These may be expressed behaviourally as changes in meal patterns, snacking behaviour and food choice. Within the next 20 years it is certain that clinicians will have a new range of anti-obesity compounds available to choose from. Such novel compounds may act on a single component of the appetite system or target a combination of these components detailed in this review. Such compounds used in combination with lifestyle changes and dietary intervention may be useful in dealing with the rising world epidemic of obesity.

L228 ANSWER 44 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999200429 EMBASE
TITLE: New approaches in the pharmacological treatment of obesity.
AUTHOR: Leonhardt M.; Hrupka B.; Langhans W.
CORPORATE SOURCE: Dr. M. Leonhardt, Institute of Animal Sciences, Swiss Federal Inst. of Technology, ETII-Zentrum/LFW, Universitatsstrasse 2, CH-8092 Zurich, Switzerland
SOURCE: European Journal of Nutrition, (1999) 38/1 (1-13).
Refs: 168
ISSN: 1436-6207 CODEN: EJNUFZ
COUNTRY: Germany
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Many new substances are currently being investigated for their usefulness in the pharmacotherapy of obesity. Most drugs interfere with monoamine neurotransmitter (serotonin, noradrenalin, dopamine and histamine) effects and act as an appetite suppressant. Other approaches are to primarily increase thermogenesis (e.g. .beta.3-adrenoceptor agonists), or to decrease fat absorption by inhibiting the pancreatic lipase (orlistat). New promising agents are substances that increase the effect of corticotropin releasing factor (CRF) or urocortin in the brain (CRF-binding protein ligand inhibitor) and a neuropeptide Y (NPY) Y5 receptor antagonist. The clinical relevance of leptin in the therapy of obesity is probably limited, but can not be fully evaluated at the moment. As obesity has a multifactorial basis, all these substances have in common the fact that they can not cure obesity. They should only be used as an adjunct to classical strategies like diet and exercise in severe obesity. For developing new, perhaps even more specific pharmacological agents, further research is needed to understand the individually different genetic and physiological basis of obesity.

L228 ANSWER 45 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998050341 EMBASE
TITLE: ARL 15849: A selective CCK-A agonist with anorectic activity in the rat and dog.
AUTHOR: Simmons R.D.; Kaiser F.C.; Pierson M.E.; Rosamond J.R.

CORPORATE SOURCE: R.D. Simmons, Pharmacology Department, Astra Arcus USA, P.O. Box 20890, Rochester, NY 14602, United States
SOURCE: Pharmacology Biochemistry and Behavior, (1998) 59/2 (439-444).
Refs: 26
ISSN: 0091-3057 CODEN: PBBHAU
PUBLISHER IDENT.: S 0091-3057(97)00446-2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
032 Psychiatry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cholecystokinin octapeptide (CCK-8) and the peptide analog ARL 14294, formerly FPL 14294, [Hpa(SO3H)-Met-Gly-Trp-Met-Asp-N(Me)Phe-NH2], have been reported to induce satiety by interaction with the CCK-A receptor subtype. ARL 15849 [Hpa(SO3H)-Nle-Gly-Trp-Nle-N(Me)-Asp-Phe-NH2] is an improved ARL 14294 analog with enhanced CCK-A receptor selectivity, greater stability, and a longer duration of action. The affinity of ARL 15849 for the CCK-A receptor (K(i) = 0.034 nM) is 6,600 fold greater than for the CCK-B receptor (K(i) = 224 nM), whereas CCK-8 and ARL 14294 are nonselective. Although comparable in potency to contract isolated gallbladder and induce pancreatic phosphatidylinositol hydrolysis, ARL 15849 is 3- and 100-fold more potent than ARL 14294 and CCK-8, respectively, to inhibit 3-h feeding in rats. The duration of feeding inhibition was significantly longer for ARL 15849 (>5 h), compared to equipotent doses of ARL 14294 (3 h), and CCK-8 (1 h). Intranasal administration of ARL 15849 inhibits feeding in beagle dogs with a greater separation between doses that induce emesis and those that inhibit feeding. Therefore, ARL 15849 is a potent, selective, intranasally active anorectic agent which may be useful in the treatment of eating disorders.

L228 ANSWER 46 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998217377 EMBASE
TITLE: [Perspectives in drug treatments of obesity].
DES PERSPECTIVES DANS LES TRAITEMENTS MEDICAMENTEUX DE L'OBESITE.
AUTHOR: Ziegler O.; Guerci B.; Meyer L.; Drouin P.
CORPORATE SOURCE: O. Ziegler, Service de Diabetologie, Maladies Metaboliques Nutrition, Hopital Jeanne d'Arc, BP 303, F-54201 Toul Cedex, France
SOURCE: Cahiers de Nutrition et de Dietetique, (1998) 33/3 (154-160).
Refs: 39
ISSN: 0007-9960 CODEN: CNDQA8
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French
SUMMARY LANGUAGE: English; French
AB As with other chronic diseases' is likely a role for pharmacological interventions in weight management program, although there is no current consensus on anorexigenic drugs in clinical practice. It is recognised that drugs are effective and have a role in the treatment of obesity, but drugs must be safe, with a high benefit to risk ratio. The use of anorexic drugs has been associated with the development of primary pulmonary hypertension. Cases of valvular heart disease associated with the

combination of fenfluramine and phentermine have been recently reported. Fenfluramines were withdrawn from the market in September 1997 at the request of the Food and Drugs Administration and the French <<Agence du medicament>>. Two compounds, Sibutramine (Meridia.RTM.) and Orlistat (Xenical.RTM.) could be considered for approval this year. The results of genetic research, as well as studies in molecular cell biology and neurobiology are expected to suggest approaches.

L228 ANSWER 47 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998132335 EMBASE
TITLE: Pharmacological and pathophysiological modulation of food intake and forestomach motility in small ruminants.
AUTHOR: Van Miert A.S.J.; Van Duin C.T.M.
CORPORATE SOURCE: A.S.J.P.A.M. Van Miert, Dept. of Veterinary Basic Sciences, Division Pharmacology, Pharmacy and Toxicology, PO Box 80176, NL-3508 TD Utrecht, Netherlands
SOURCE: Journal of Veterinary Pharmacology and Therapeutics, (1998) 21/2 (1-17).
Refs: 200
ISSN: 0140-7783 CODEN: JVPTD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English

L228 ANSWER 48 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998028866 EMBASE
TITLE: Synthesis and biological evaluation of potent, selective, hexapeptide CCK-A agonist anorectic agents.
AUTHOR: Pierson M.E.; Comstock J.M.; Simmons R.D.; Kaiser F.; Julien R.; Zongrone J.; Rosamond J.D.
CORPORATE SOURCE: M.E. Pierson, Astra Arcus USA, P.O. Box 20890, Rochester, NY 14602, United States
SOURCE: Journal of Medicinal Chemistry, (1997) 40/26 (4302-4307).
Refs: 27
ISSN: 0022-2623 CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cholecystokinin (CCK) is a 33-amino acid peptide with multiple functions in both the central nervous system (via CCK-B receptors) and the periphery (via CCK-A receptors). CCK mediation of satiety via the A-receptor subtype suggest a role for CCK in the management of obesity. The carboxy terminal octapeptide (CCK-8) is fully active in this regard, but is lacking in receptor selectivity, metabolic stability, and oral bioavailability. Inversion of the chirality of Asp7 in conjunction with N-methylation of Phe8 produces compound 5 which exhibits high affinity and 2100-fold selectivity for CCK-A receptors. Compound 6 (Hpa(SO3H)-Nle-Gly-Trp-Nle-MeAsp-Phe-NH2), derived from moving the N-methyl group from Phe to Asp, decreased CCK-B affinity substantially without affecting CCK-A affinity, giving a compound with 6600-fold selectivity for CCK-A receptors. These compounds inhibit food intake with nanomolar potency following intraperitoneal administration in fasted rats. In addition to greater potency, compound 6 produces weight loss in rats when administered over nine consecutive days. Intranasal administration of 6 potently inhibits feeding in beagle dogs. Compound 6 produces potent anorectic activity via the CCK-A receptor system.

L228 ANSWER 49 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97312121 EMBASE
DOCUMENT NUMBER: 1997312121
TITLE: [Healthy weight loss: A guideline for the treatment of obesity].
GEZOND VERMAGEREN. EEN RICHTLIJN VOOR HET BEHANDELEN VAN OVERGEWICHT.
AUTHOR: Vervaet M.; Bogaert M.; Van Gaal L.; Van Winckel M.; Borms J.
CORPORATE SOURCE: M. Vervaet, Psychiatrie en Neuropsychologie, Universitair Ziekenhuis, Gent, Belgium
SOURCE: Tijdschrift voor Geneeskunde, (1997) 53/19 (1269-1281).
Refs: 35
ISSN: 0371-683X CODEN: TGEKBW
COUNTRY: Belgium
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: Dutch
SUMMARY LANGUAGE: Dutch

L228 ANSWER 50 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97189565 EMBASE
DOCUMENT NUMBER: 1997189565
TITLE: The pharmacologic approach to the treatment of obesity.
AUTHOR: Weiser M.; Frishman W.H.; Michaelson M.D.; Abdeen M.A.
CORPORATE SOURCE: Dr. W.H. Frishman, Jack D. Weiler Hospital, Albert Einstein College of Medicine, Montefiore Medical Center, 1825 Eastchester Road, Bronx, NY 10461, United States
SOURCE: Journal of Clinical Pharmacology, (1997) 37/6 (453-473).
Refs: 259
ISSN: 0091-2700 CODEN: JCPCBR
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Obesity is a major risk factor for morbidity and mortality, and a series of pharmacologic approaches are available for helping to manage the problem. Obesity is caused by an imbalance between caloric intake and energy expenditure, which is influenced by both environmental and genetic factors. Pharmacologic treatments include anorexigenic agents, which fall into two broad categories: those that act via bruin catecholamine pathways and those that act via serotonin pathways. The most recent oral agents approved are dexfenfluramine, which is currently being marketed, and sibutramine. Both agents inhibit the control reuptake of serotonin but in addition many have effects on thermogenesis. Under investigation are agents that increase energy expenditure: the .beta.3-adrenergic receptor agonists and drugs that prevent the intestinal absorption of free fatty acids and cholesterol. In development are innovative approaches to influence leptin and its receptors, various obesity genes, and biologic substances thought to influence satiety (neuropeptide Y, enterostatin, cholecystokinin, bombesin, and amylin). Obesity has now become a major target for drug development not only for affecting obesity per se but also for managing and preventing comorbid conditions such as diabetes and cardiovascular disease.

L228 ANSWER 51 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998006774 EMBASE
TITLE: Advances and retreats in the pharmacotherapy of obesity.

AUTHOR: Davis W.M.; Feller D.R.
CORPORATE SOURCE: Dr. W.M. Davis, Dept. of Pharmacol./Natl. Ctr., Development of Natural Products, Res. Inst. of Pharmaceutical Sci., Mississippi, MS, United States
SOURCE: Drug Topics, (1997) 141/23 (114-121).
ISSN: 0012-6616 CODEN: DGTNA7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L228 ANSWER 52 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96346939 EMBASE
DOCUMENT NUMBER: 1996346939
TITLE: Alternate drug delivery routes for A-71623, a potent cholecystokinin-A receptor agonist tetrapeptide.
AUTHOR: Cannon J.B.; Akwete Adjei L.; Fu Lu M.-Y.; Garren K.
CORPORATE SOURCE: Abbott Laboratories, 100 Abbott Park Road,Abbott Park, IL 60064-3500, United States
SOURCE: Journal of Drug Targeting, (1996) 4/2 (69-78).
ISSN: 1061-186X CODEN: JDTAEH
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

L228 ANSWER 53 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95267576 EMBASE
DOCUMENT NUMBER: 1995267576
TITLE: Pharmacological aspects of obesity treatment: Towards the 21st century.
AUTHOR: Blundell J.E.; Halford J.C.G.
CORPORATE SOURCE: BioPsychology Group, Psychology Department, University of Leeds,Leeds LS2 9JT, United Kingdom
SOURCE: International Journal of Obesity, (1995) 19/SUPPL. 3 (S51-S55).
ISSN: 0307-0565 CODEN: IJOBDP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB OBESITY: A BIG-BEHAVIOURAL-ENVIRONMENTAL PHENOMENON : Obesity is on the increase all over the world in technologically advanced countries, developing countries and rural communities. What is causing this upward drift in body weight? Can drugs do anything to ameliorate the situation? It is generally agreed that obesity results from genetic vulnerability combined with a provocative environmental situation. This provides the basis for a psychobiological interaction in which behaviour plays a key role. This is the case since it is behaviour which translates biological propensities into action on the environment, and it is behaviour which mediates (in part) the effect of the environment upon biology. Two particularly important behavioural aspects of the genes-environment

interaction are low levels of physical activity (high sedentariness) and dietary habits which favour overconsumption (high intake of energy, particularly as fat). One continuing theme of research is the development of drugs to allow people to gain control over appetite by modifying eating patterns (dietary habits) through a number of possible mechanisms. The use of drugs to make people more willing or more able to engage in physical activity is not widely discussed although the use of drugs to increase total energy expenditure (via a variety of mechanisms) is actively researched. More than a decade ago Sullivan defined the framework for the development of anti-obesity drugs by specifying that drugs could act on energy intake, energy output or on those mechanisms involved in the assimilation and storage of lipids in the body. Consequently the range of possible actions of anti-obesity drugs extends from the adjustment of habitual patterns of behaviour to an action on the genetic transcription of molecules regulating the biochemistry of adipocytes. Additionally, other writers have set out the optimal properties for an anti-obesity drug. These should include a suppression of energy intake. reduction in body fat mass, preservation of lean body tissue and an ergogenic action which would at least prevent the decline in resting metabolic rate which may occur with food restriction. Is there currently a drug that meets these criteria or could such a drug ever be developed?

L228 ANSWER 54 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94042445 EMBASE
DOCUMENT NUMBER: 1994042445
TITLE: Ligands for cholecystokinin receptors: Recent developments.
AUTHOR: Trivedi B.K.
CORPORATE SOURCE: Parke-Davis Pharmaceutical Res Div, Warner Lambert Company, 2800 Plymouth Road,Ann Arbor, MI 48105, United States
SOURCE: Current Opinion in Therapeutic Patents, (1994) 4/1 (31-44). ISSN: 0962-2594 CODEN: COTPES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L228 ANSWER 55 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93094204 EMBASE
DOCUMENT NUMBER: 1993094204
TITLE: Pharmacologic treatment of obesity.
AUTHOR: Hendler R.
CORPORATE SOURCE: Division of Endocrinology, Department of Internal Medicine, Yale University School of Medicine, 333 Cedar Street,New Haven, CT 06510-8056, United States
SOURCE: Current Opinion in Gastroenterology, (1993) 9/2 (298-303). ISSN: 0267-1379 CODEN: COGAEK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Obesity is a chronic metabolic disorder. Genetic and environmental factors contribute to its development and maintenance. The effectiveness of different treatments in reducing weight and their ability to maintain weight loss is minimal. This paper reviews new developments in the pharmacologic approach to the treatment of obesity in addition to diet, exercise, and behavior modification.

L228 ANSWER 56 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-175054 [17] WPIDS

DOC. NO. CPI: C2003-045680
TITLE: New fused heterocyclic compounds useful for treatment of e.g. obesity.
DERWENT CLASS: B02
INVENTOR(S): CHEN, X; DAI, K; FAN, P; HUANG, S; LI, L; MIHALIC, J T
PATENT ASSIGNEE(S): (TULA-N) TULARIK INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002089729	A2	20021114	(200317)*	EN	61
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
US 2003023085	A1	20030130	(200317)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002089729	A2	WO 2002-US13856	20020503
US 2003023085	A1 Provisional	US 2001-288665P	20010504
		US 2002-138279	20020503

PRIORITY APPLN. INFO: US 2001-288665P 20010504; US 2002-138279 20020503

AB WO 200289729 A UPAB: 20030312

NOVELTY - Fused heterocyclic compounds are new.

DETAILED DESCRIPTION - Fused heterocyclic compounds of formula (I) and their salts and prodrugs are new.

A, B' = CR' or N;

R' = H, 1-5C alkyl, arylalkyl, -C(O)R7, -CO2R8 or -C(O)NR5R6;

V' = bond or t;

t = -O-, -S-, -C(O)-, -N(R1)- or -N=;

R1 = H or 1-5C alkyl;

W' = t or -C(S)-;

Z = -N(R)-, -N(R)-1-3C alkylene or 1-3C alkylene-N(R)-1-3C alkylene;

R = H, 1-7C alkyl, heterocycloalkyl(1-7C)alkyl, aryl, arylalkyl, -C(O)R7, -CO2R8, -C(O)NR5R6, -S(O)mNR5R6 or -S(O)mR7;

R1 = H, halo, 1-5C alkyl, perfluoro-1-5C alkyl, -OR2, -SR2, aryl, arylalkyl, -NO2, -NR5R6, -C(O)R7, -CO2R8 -C(O)NR5R6, -N(R5)C(O)R7, -N(R5)CO2R9, -N(R7)C(O)NR5R6, -S(O)mNR5R6, -S(O)mR7, -CN or -N(R5)S(O)mR9;

R2 = R1, aryl or aryl-1-5C alkyl;

R2, R3 = t' or =O;

t' = H, -OR2, -CN, 1-5C alkyl or aryl;

R4 = t', -C(O)R7, -CO2R8 or -C(O)NR5R6;

R9 = (aryl)alkyl or aryl;

R5 - R8 = H or R9;

R5+R6 = 4 - 8 membered ring containing 1 - 3 heteroatoms;

m = 1 - 2;

n = 0 - 8;

Ar = single or fused (hetero)aryl ring containing 1 - 4 heteroatoms selected from N, O and S.

provided that R2 is not H when Ar is benzene, A and B' are both CH, V' is a bond, W' is -N(R1)- and Z is -NR-CH2-.

An INDEPENDENT CLAIM is included for a composition comprising (I) and a carrier or excipient.

ACTIVITY - **Anorectic**; Anabolic; Tranquilizer; Antidepressant; Cardiant; Hypotensive; Antilipemic; Antidiabetic.

MECHANISM OF ACTION - **Melanin-concentrating hormone** receptor (MCHR) antagonist/**agonist** (claimed).

The compounds were tested for MCHR modulatory activity according to Lembo et al. (1999) Nature Cell biol. 1:267 - 271. No results given.

USE - For treating obesity, an eating disorder e.g. anorexia nervosa, an anxiety disorder e.g. anxiety, panic disorder and obsessive-compulsive disorder, and mood disorder e.g. depression; for modifying eating behavior where food intake is decreased or increased (claimed); for treating cardiovascular disorders, lipid disorders and metabolic disorders e.g. hypertension, hyperlipidemia, coronary artery disease and diabetes, bulimia or euphoria.

Dwg.0/1

L228 ANSWER 57 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-479743 [51] WPIDS
DOC. NO. CPI: C2002-136550
TITLE: New tripeptidyl peptidase inhibitors, useful in treating eating disorders, obesity, psychotic syndromes or associated psychiatric disorders.
DERWENT CLASS: B03
INVENTOR(S): BRESLIN, H J; DE WINTER, H L J; KUKLA, M J
PATENT ASSIGNEE(S): (JANC) JANSSEN PHARM NV
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002036116	A2	20020510	(200251)*	EN	50

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002024797 A 20020515 (200258)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002036116	A2	WO 2001-EP12388	20011024
AU 2002024797	A	AU 2002-24797	20011024

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002024797	A Based on	WO 200236116

PRIORITY APPLN. INFO: US 2000-244223P 20001030

AB WO 200236116 A UPAB: 20030603

NOVELTY - Tripeptidyl peptidase inhibitors are new.

DETAILED DESCRIPTION - Tripeptidyl peptidase inhibitor of formula (I) or their isomeric forms or acid addition salts are new.

n = 0 or 1;

X = O, S or (CR4R5)m;

m = 1 or 2;

R4 and R5 = H or 1-4C alkyl;

R1 = 1-6C alkylcarbonyl (optionally substituted by OH), 1-6C alkyloxycarbonyl, amino(1-6C) alkylcarbonyl (in which 1-6C alkyl is optionally substituted by 3-6C cycloalkyl), mono- or di-(1-4C

alkyl)amino-(1-6C) alkylcarbonyl, aminocarbonyl (substituted with aryl), 1-6C alkylcarbonyloxy(1-6C) alkylcarbonyl, 1-6C alkyloxycarbonylamino(1-6C) alkylcarbonyl (in which the amino group is optionally substituted by 1-4C alkyl), an amino acid residue bound via the carbonyl group or 1-6C alkyl (substituted with amino or arylcarbonyl);

R2 = benzimidazole (optionally mono- or di-substituted by halo, trifluoromethyl, 1-4C alkyl, OH, hydroxycarbonyl or 1-4C alkyloxycarbonyl), (R7)m' pyrrol-2-yl (substituted by R6 on 1 position), (R7)m' imidazol-2-yl (substituted by R6 on 1 position), (R7)m' imidazol-5-yl (substituted by R6 on 1 position), (1,2,4)triazol-5-yl (substituted by R6 on 4 position and by R7 on 3-position), (R7)m' oxazol-2-yl, (R7)m' thiazol-2-yl or (1,2,4)oxadiazol-3-yl (substituted by R7 on 5 position);

m' = 1 or 2;

R6 = H or 1-4C alkyl;

R7 = H, halo, amino, OH, trifluoromethyl, 1-6C alkyl, 1-4C alkyl (substituted by OH, hydroxycarbonyl, 1-4C alkyloxycarbonyl, aminocarbonyl, mono- or di-(1-4C alkyl)aminocarbonyl, amino, mono- or di-(1-4C alkyl)amino), Ph, hydroxycarbonyl, 1-4C alkyloxycarbonyl, 1-4C alkylcarbonyl or 1-4C alkyloxycarbonyl(1-4C)alkylaminocarbonyl;

R3 = radical of formulae (a), (b) or (c) (all optionally mono- or tri-substituted by T, amino or phenyl (optionally mono- or di-substituted by T)) or CH2CH2 (optionally substituted by halo or phenylmethyl);

T = halo, OH, 1-6C alkyl, 1-6C alkyloxy, nitro, cyano or trifluoromethyl; and

aryl = phenyl (optionally substituted by amino, nitro or hydroxycarbonyl).

INDEPENDENT CLAIMS are included for:

(1) Composition comprising a mixture of (I) and a carrier; and

(2) Preparation of (I).

ACTIVITY - **Anorectic.**

No biological data available.

MECHANISM OF ACTION - Tripeptidyl peptidase inhibitor (preferably **tripeptidyl peptidase II** (TPP II) inhibitor); delta -Opioid receptor binder.

TPP II activity was evaluated using AAF-AMC as a TPP II substrate in a potassium phosphate buffer pH 7.5 with DTT (1 mM) and EGTA (1 mM). 2,3-Dihydro- beta -oxo-2-(5-propyl-1,2,4-oxadiazol-3-yl)-1H-1-ethanamine trifluoroacetate (A) was added at a final dimethylsulfoxide (DMSO) concentration of 1%. Fluorescence was measured at 405 nm.

The IC50 value of (A) was at most 1.10-5 M.

USE - (I) is used as medicine (claimed) for treating eating disorders, obesity, psychotic syndromes or associated psychiatric disorders.

ADVANTAGE - (I) inhibits membrane tripeptidyl peptidase responsible for inactivation of endogenous neuropeptides such as cholecystokins. (I) also exhibits opioid activity such as delta -opioid, mu -opioid and/or kappa-opioid activity.

Dwg.0/0

L228 ANSWER 58 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-471444 [50] WPIDS
DOC. NO. CPI: C2002-134073
TITLE: Composition comprising human stresscopin 1 or stresscopin 2 polypeptide, useful in **appetite suppression**, for cardioprotection, reducing edema, reducing inflammation, organ graft rejection, reducing hypertension.
DERWENT CLASS: B04 D16
INVENTOR(S): HSU, S Y; HSUEH, A J W
PATENT ASSIGNEE(S): (HSUS-I) HSU S Y; (HSUE-I) HSUEH A J W; (STRD) UNIV LELAND STANFORD JUNIOR
COUNTRY COUNT: 23

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002034934 A2		20020502	(200250)*	EN	50
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU CA JP					
US 2002082409 A1		20020627	(200250)		
AU 2002011717 A		20020506	(200257)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002034934 A2		WO 2001-US32065	20011010
US 2002082409 A1	Provisional	US 2000-244128P	20001026
	Provisional	US 2001-276615P	20010315
		US 2001-682706	20011009
AU 2002011717 A		AU 2002-11717	20011010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002011717 A	Based on	WO 200234934

PRIORITY APPLN. INFO: US 2001-276615P 20010315; US 2000-244128P 20001026; US 2001-682706 20011009

AB WO 200234934 A UPAB: 20020807

NOVELTY - Composition (I) comprising stresscopin peptide which has at least 18 contiguous amino acids of fully defined sequence of 112 (S2), 43 (S3), 161 (S5) or 40 (S6) amino acids (aa) given in specification, where (S2) and (S3) are aa sequence (AS) of human stresscopin 1 precursor protein and mature protein respectively, and (S5) and (S6) are AS of human stresscopin 2 precursor protein and mature protein respectively.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid molecule (II) comprising a cDNA sequence encoding a mammalian stresscopin protein that will hybridize under stringent conditions to a fully defined sequence of 339 (S1) or 486 (S4) nucleotides as given in specification, or which encodes a peptide having a sequence of (S3) or (S6);

(2) an antibody (III) that specifically recognizes stresscopin peptide;

(3) a non-human transgenic animal model (IV) of stresscopin gene function, where the transgenic animal comprises an introduced alteration in a stresscopin gene;

(4) screening (M1) for a biologically active agents that modulate stresscopin function, involves combining a candidate biologically active agent with any one of a mammalian stresscopin peptide; a cell comprising a nucleic acid encoding a mammalian stresscopin peptide; or a non-human transgenic model for stresscopin gene function comprising one of:

(a) a knockout of an stresscopin gene;

(b) an exogenous and stably transmitted mammalian stresscopin gene sequence; and determining the effect of the agent on stresscopin function.

ACTIVITY - Antiinflammatory; antiarthritic; antigout; antipsoriatic; antirheumatoid; vulnerary; dermatological; cardiant; vasotropic; anorectic; hypotensive; tranquilizer; immunosuppressive; antiasthmatic.

The antiinflammatory effect of stresscopin and related peptides were assayed using an established model. 5-week-old male Sprague-Dawley rats were injected with 20 nM of the testing peptide and anesthetized with ketamine (1 mg/kg). Thirty minutes, later, paw edema was induced following a one minute exposure to hot water at 58 deg. C. The animals were

sacrificed 30 minutes later. Both paws were removed at the ankle joint and weighed. The degree of edema was estimated as the differences in weight gain between the heated and uninjected paw divided by the weight of the unheated paw. Results showed that intraperitoneal administration with stresscopin 1 or stresscopin 2 suppressed heat-induced edema formation in anesthetized rats, similar to that induced by urocortin and corticotrophin releasing hormone (CRH).

MECHANISM OF ACTION - Activator of **corticotropin releasing** hormone receptor 2 (CRH-R2), without inducing adrenocorticotrophic hormone (ACTH); stresscopin polypeptide function or expression modulator; gene therapy.

USE - (I) is useful in a method of appetite suppression, for cardioprotection, reducing edema, reducing inflammation, organ graft rejection, reducing hypertension, treating stress related to trauma, and treating affective disorders (claimed). (II) is useful for expressing stresscopin polypeptides which are useful in recovery phase of stress responses, as an antiinflammatory agent, as a hypotensive agent, as a cardioprotective agent, and in the treatment of psychiatric and anxiolytic disorders, and for screening for biologically active agents that act in **corticotropin releasing** hormone (CRH) signaling pathways. (II), and its corresponding genes, gene products, antisense nucleotides and (III) are useful in diagnostics and therapeutics. (II) is also useful for identifying homologous of related genes, and for producing compositions that modulate the expression of the encoded protein, for gene therapy, mapping functional regions of the protein, and in studying associated physiological pathways.

(M1) is useful for identifying agents that modulate stresscopin functions. The compounds with the desired pharmacological activity may be administered to a host for treatment of stress related disorders, etc. The compounds may also be used to enhance stresscopin function in weight reduction, treatment of heart disease, reduction of edema, suppression of anxiety, stress reduction following major surgery. Stresscopins encoded by (II) are administered to obese patients for purposes of appetite suppression. The polypeptides are also useful for promoting gastric stasis and anorexic behavior without concomitant activation of the adrenocorticotrophic hormone (ACTH)-glucocorticoid axis, inhibiting excessive release of ACTH, treating dysthymia which is a chronic disorder characterized by symptoms that include poor appetite or overeating, low energy (decreased arousal), insomnia or hypersomnia, and poor concentration, and for reducing arterial blood pressure, enhancing the stress coping responses, ameliorating ischemic injury or myocardial infarct size consequent to myocardial ischemia, treating different skin diseases, treating both the early and late stages of inflammatory arthritis, as well as non-infectious inflammatory arthropathy such as rheumatoid arthritis, bursitis, tendinitis, soft tissue injuries, Sjogren's syndrome, system lupus erythematosus, psoriatic arthritis, gout and other crystalline arthropathies, capsulitis, carpal tunnel syndrome, myositis, polymyalgia, rheumatica, synovitis and Reiter's syndrome, treating edema secondary to brain tumors or irradiation for cancer, edema resulting from stroke, head trauma or spinal cord injury, post-surgical edema, asthma.

(II) is useful in the treatment of the above mentioned disorders by gene therapy techniques. DNA-based reagents derived from the sequence of stresscopins, e.g. polymerase chain reaction (PCR) primers, oligonucleotide or cDNA probes, as well as antibodies against stresscopins, are used to screen patient samples, e.g. biopsy-derived tissues, blood samples, etc. for amplified stresscopin DNA, or increased expression of stresscopin mRNA or proteins. DNA-based reagents are designed for evaluation of chromosomal loci implicated in certain diseases e.g. for use in loss-of-heterozygosity (LOH) studies, or design of primers based on stresscopin coding sequence. The polynucleotides can be used to detect differences in expression levels between two samples. The nucleic acid and/or polypeptide compositions may be used to analyze a patient

sample for the presence of polymorphisms associated with a disease state or genetic predisposition to a disease state.
Dwg.0/4

L228 ANSWER 59 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-335784 [35] WPIDS
DOC. NO. CPI: C2001-103711
TITLE: Use of a growth hormone to **suppress appetite** or induce satiety.
DERWENT CLASS: B04
INVENTOR(S): JEPSEN, H; MALMLOEF, K
PATENT ASSIGNEE(S): (NOVO) NOVO NORDISK AS
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001032200	A1	20010510	(200135)*	EN	28

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001011305 A 20010514 (200149)
EP 1229927 A1 20020814 (200261) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001032200	A1	WO 2000-DK600	20001027
AU 2001011305	A	AU 2001-11305	20001027
EP 1229927	A1	EP 2000-972638	20001027
		WO 2000-DK600	20001027

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001011305	A	Based on	WO 200132200
EP 1229927	A1	Based on	WO 200132200

PRIORITY APPLN. INFO: US 1999-165491P 19991115; DK 1999-1585 19991103

AB WO 200132200 A UPAB: 20010625
NOVELTY - Use of a growth hormone (GH) in the manufacture of a medicament for appetite suppression or satiety-induction.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a method of preventing or treating diseases associated with impaired appetite regulation comprising the administration of a growth hormone; and
(2) a pharmaceutical composition comprising a growth hormone in combination with an anti-diabetic agent or another appetite-suppressing or satiety-inducing agent, and a carrier or excipient.
ACTIVITY - Anorectic; antidiabetic; hypotensive; antiarteriosclerotic; antilipemic; cardiant; osteopathic; antiarthritic.
Rats fed high fat diets before and low fat diets during the test period (21 days), and treated with saline (control) ate 28.2 g/kg/day. Rats fed the same diet but treated with 4 mg/kg/day human growth hormone ate 15.9 g/kg/day and those treated with 4 mg/kg/day rat growth hormone

ate 10.0 g/kg/day.
MECHANISM OF ACTION - None given.
USE - For suppressing appetite in obese individuals and treating disorders associated with impaired appetite regulation e.g. obesity, bulimia, type II diabetes, atherosclerosis, hypertension, dyslipidaemia, coronary heart disese and osteoarthritis.
Dwg.0/6

L228 ANSWER 60 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-475832 [41] WPIDS
DOC. NO. CPI: C2000-142672
TITLE: Screening methods for compounds as SLC-1 (ant)agonists useful in the treatment of eating disorders and as preventives and remedies for e.g. atonic bleeding and Prader-Willi syndrome.
DERWENT CLASS: B04 D16
INVENTOR(S): ISHIBASHI, Y; KITADA, C; MORI, M; SHIMOMURA, Y; SUGO, T; SUZUKI, N; TAKEKAWA, S
PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000040725	A1	20000713	(200041)*	JA	123
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AU AZ BA BB BG BR BY CA CN CR CU CZ DM EE GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT LV MA MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT TZ UA UZ VN YU ZA					
AU 2000018020	A	20000724	(200052)		
JP 2001141728	A	20010525	(200136)		44
EP 1143000	A1	20011010	(200167)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2000592421	X	20020423	(200243)		
CN 1344321	A	20020410	(200249)		
KR 2002008111	A	20020129	(200253)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000040725	A1	WO 1999-JP7336	19991227
AU 2000018020	A	AU 2000-18020	19991227
JP 2001141728	A	JP 1999-371313	19991227
EP 1143000	A1	EP 1999-961418	19991227
		WO 1999-JP7336	19991227
JP 2000592421	X	WO 1999-JP7336	19991227
		JP 2000-592421	19991227
CN 1344321	A	CN 1999-816370	19991227
KR 2002008111	A	KR 2001-708291	20010628

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000018020	A	Based on	WO 200040725
EP 1143000	A1	Based on	WO 200040725
JP 2000592421	X	Based on	WO 200040725

PRIORITY APPLN. INFO: JP 1999-249300 19990902; JP 1998-374454 19981228; JP 1999-122688 19990428

AB WO 200040725 A UPAB: 20000831
NOVELTY - Screening components (I) or their salts that can alter the binding properties of melanin-concentrating hormone (MCH) or its derivative or salt to SLC-1 or its salt, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a kit comprising components capable of carrying out (I);
(2) compounds (II) or salts identified by (I);
(3) drugs comprising (II);
(4) a protein (III) or its salt with a fully defined 422 amino acid sequence (given in the specification);
(5) a DNA (IV) molecule encoding (III);
(6) a peptide or its salt which is a MCH derivative or a derivative of a peptide containing amino acids from positions 5 to 19 of the N-terminal of a fully defined 19 amino acid sequence (given in the specification) both obtained by using the Burton-Hunter reagent; and
(7) a compound or its salt of formula (A).
ACTIVITY - **Anorectic**; gynecological; abortifaciant; antoanemia; anabolic.
MECHANISM OF ACTION - Orphan G protein-couple receptor protein; (ant) **agonist** of **melanin-concentrating hormone** binding to SLC-1.
USE - (II) are useful as SLC-1 (ant)agonists in eating disorders and as preventives and remedies for e.g. period pains, uterine recovery failure, caesarean section, artificial interruption of pregnancy, galactostosis, tonic uterine contraction, fetal asphyxia, rupture of uterus, cervical rupture, premature birth and Prader-Willi syndrome.
Dwg.0/10

L228 ANSWER 61 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-365395 [31] WPIDS
DOC. NO. CPI: C2000-110293
TITLE: Reducing weight in obese subjects, comprises administering a **leptin** or **leptin** mimetric, and a synthetic organic **appetite suppressant**.
DERWENT CLASS: B05
INVENTOR(S): ARONNE, L J
PATENT ASSIGNEE(S): (ARON-I) ARONNE L J
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000025806	A1	20000511	(200031)*	EN	9

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000025806	A1	WO 1999-US26169	19991104

PRIORITY APPLN. INFO: US 1998-186877 19981104
AB WO 200025806 A UPAB: 20000630
NOVELTY - A method of reducing obesity, comprises combined administration of **leptin** or a **leptin** mimetric, and a synthetic organic appetite suppressing compound, is new.
DETAILED DESCRIPTION - The compounds are administered in a dosage to suppress the appetite and maintain the subjects **leptin** levels at a level which will sustain continued weight reduction.

ACTIVITY - Anorectic.
MECHANISM OF ACTION - None given.
USE - The method is used to reduce the weight of obese subjects (claimed).
ADVANTAGE - A **leptin** is administered at the same time as the appetite suppressant, to overcome the problem of a weight loss plateau, where the patient cannot lose more weight despite considerable effort.
Dwg.0/0

L228 ANSWER 62 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1999-315250 [27] WPIDS
DOC. NO. CPI: C1999-093223
TITLE: Composition for treating obesity and diabetes comprises a specific beta-3 agonist and an **anorectic** agent.
DERWENT CLASS: B02 B03 C02
INVENTOR(S): DOW, R L
PATENT ASSIGNEE(S): (PFIZ) PFIZER PROD INC
COUNTRY COUNT: 30
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 920864	A1	19990609	(199927)*	EN	20
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 9896055	A	19990624	(199936)		
HU 9802795	A2	19990830	(199940)		
JP 11228447	A	19990824	(199944)		17
CA 2255318	A1	19990603	(199947)	EN	
KR 99062718	A	19990726	(200043)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 920864	A1	EP 1998-309273	19981112
AU 9896055	A	AU 1998-96055	19981202
HU 9802795	A2	HU 1998-2795	19981202
JP 11228447	A	JP 1998-335819	19981126
CA 2255318	A1	CA 1998-2255318	19981201
KR 99062718	A	KR 1998-52532	19981202

PRIORITY APPLN. INFO: US 1997-67268P 19971203
AB EP 920864 A UPAB: 19991122
NOVELTY - Composition comprises a compound which modifies eating behavior or prodrug or its salt and (4-(2-(2-(6-aminopyrid-3-yl)-2(R)-hydroxyethylamino)ethoxy)phenyl)acetic acid (I) or their salts or prodrugs.
DETAILED DESCRIPTION - (4-(2-(2-(6-aminopyrid-3-yl)-2(R)-hydroxyethylamino)ethoxy)phenyl)acetic acid is of formula (I).
An INDEPENDENT CLAIM is also included for a kit comprising:
(a) an amount of a compound which modifies eating behaviour, or its salt or prodrug in a first unit dosage form;
(b) an amount of (I) or its salt or prodrug; and
(c) a container.
ACTIVITY - Anorectic; antidiabetic.
MECHANISM OF ACTION - NPY antagonist; CCK-A agonist; monoamine uptake inhibitor; sympathomimetic; serotoninergic; dopamine agonist; melanocyte-stimlating hormone receptor agonist; cannabinoid receptor antagonist; melanocyte-stimulating hormone; melanin concentrating hormone **antagonist; galanin antagonist.**

USE - The composition is useful for treating eating disorders particularly obesity in animals and humans and diabetes.

ADVANTAGE - The composition is an effective treatment for obesity and diabetes in both humans and animals.

Dwg.0/0

L228 ANSWER 63 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1998-609904 [51] WPIDS
DOC. NO. CPI: C1998-182737
TITLE: New **appetite suppressant** steroid glycoside compounds - are extracts of plants of genus Trichocaulon or Hoodia or their analogues, used for treating obesity.
DERWENT CLASS: B01
INVENTOR(S): HORAK, R M; LEARMONTH, R A; MAHARAJ, V; VLEGGAAR, R; WHITTAL, R D; VAN HEERDEN, F R
PATENT ASSIGNEE(S): (COUL) CSIR; (ABRA-I) ABRAMS M J; (COUL) CSIR CORP BUILDING
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9846243	A2	19981022	(199851)*	EN	162
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9870613	A	19981111	(199912)		
GB 2338235	A	19991215	(200001)		
ZA 9803170	A	19991229	(200006)		164
NO 9904992	A	19991214	(200009)		
EP 973534	A1	20000126	(200010)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI					
CZ 9903599	A3	20000517	(200031)		
BR 9808593	A	20000523	(200035)		
CN 1252000	A	20000503	(200036)		
JP 2000510482	W	20000815	(200044)		150
SK 9901418	A3	20000912	(200055)		
HU 2000000838	A2	20001030	(200064)		
KR 2001006424	A	20010126	(200152)		
GB 2360519	A	20010926	(200156)		
GB 2360520	A	20010926	(200156)		
GB 2338235	B	20011114	(200169)		
GB 2360520	B	20011107	(200169)		
GB 2360519	B	20011128	(200202)		
US 6376657	B1	20020423	(200232)		
MX 9909443	A1	20010701	(200236)		
AU 746414	B	20020502	(200238)		
AU 2002026125	A	20020509	(200238)#		
AU 2002026126	A	20020509	(200238)#		
EP 1213020	A2	20020612	(200239)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI					
NZ 337422	A	20020531	(200246)		
EP 1222927	A2	20020717	(200254)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI					
JP 2002205997	A	20020723	(200263)		68
US 2002168427	A1	20021114	(200277)		

JP 2003026591 A 20030129 (200319) 59

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9846243	A2		WO 1998-GB1100	19980415
AU 9870613	A		AU 1998-70613	19980415
GB 2338235	A		WO 1998-GB1100	19980415
			GB 1999-19797	19990820
ZA 9803170	A		ZA 1998-3170	19980415
NO 9904992	A		WO 1998-GB1100	19980415
			NO 1999-4992	19991014
EP 973534	A1		EP 1998-917372	19980415
			WO 1998-GB1100	19980415
CZ 9903599	A3		WO 1998-GB1100	19980415
			CZ 1999-3599	19980415
BR 9808593	A		BR 1998-8593	19980415
			WO 1998-GB1100	19980415
CN 1252000	A		CN 1998-804165	19980415
JP 2000510482	W		JP 1998-543633	19980415
			WO 1998-GB1100	19980415
SK 9901418	A3		WO 1998-GB1100	19980415
			SK 1999-1418	19980415
HU 2000000838	A2		WO 1998-GB1100	19980415
			HU 2000-838	19980415
KR 2001006424	A		KR 1999-709513	19991015
GB 2360519	A	Derived from	GB 1999-19797	19990820
			GB 2001-17039	20010712
GB 2360520	A	Derived from	GB 1999-19797	19990820
			GB 2001-17041	20010712
GB 2338235	B		WO 1998-GB1100	19980415
			GB 1999-19797	19990820
GB 2360520	B	Derived from	GB 1999-19797	19990820
			GB 2001-17041	20010712
GB 2360519	B	Derived from	GB 1999-19797	19990820
			GB 2001-17039	20010712
US 6376657	B1		WO 1998-GB1100	19980415
			US 1999-402962	19991013
MX 9909443	A1		MX 1999-9443	19991014
AU 746414	B		AU 1998-70613	19980415
AU 2002026125	A	Div ex	AU 1998-70613	19980415
			AU 2002-26125	20020318
AU 2002026126	A	Div ex	AU 1998-70613	19980415
			AU 2002-26126	20020318
EP 1213020	A2	Div ex	EP 1998-917372	19980415
			EP 2002-4101	19980415
NZ 337422	A		NZ 1998-337422	19980415
			WO 1998-GB1100	19980415
EP 1222927	A2	Div ex	EP 1998-917372	19980415
			EP 2002-4100	19980415
JP 2002205997	A	Div ex	JP 1998-543633	19980415
			JP 2002-3897	19980415
US 2002168427	A1	Div ex	WO 1998-GB1100	19980415
		Div ex	US 1999-402962	19991013
			US 2002-73357	20020213
JP 2003026591	A	Div ex	JP 1998-543633	19980415
			JP 2002-184593	19980415

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9870613	A	Based on	WO 9846243
GB 2338235	A	Based on	WO 9846243
EP 973534	A1	Based on	WO 9846243
CZ 9903599	A3	Based on	WO 9846243
BR 9808593	A	Based on	WO 9846243
JP 2000510482	W	Based on	WO 9846243
HU 2000000838	A2	Based on	WO 9846243
GB 2338235	B	Based on	WO 9846243
US 6376657	B1	Based on	WO 9834624
AU 746414	B	Previous Publ.	AU 9870613
		Based on	WO 9846243
AU 2002026125	A	Div ex	AU 746414
AU 2002026126	A	Div ex	AU 746414
EP 1213020	A2	Div ex	EP 973534
NZ 337422	A	Div in	NZ 516696
		Based on	WO 9846243
EP 1222927	A2	Div ex	EP 973534
US 2002168427	A1	Div ex	US 6376657

PRIORITY APPLN. INFO: ZA 1997-3201 19970415; AU 2002-26125 20020318; AU 2002-26126 20020318

AB WO 9846243 A UPAB: 20020208

Preparation of an extract (A) having appetite suppressant activity from a plant of genus Trichocaulon or Hoodia involves treating collected plant material with a solvent to extract the active fraction, separating the extract from the rest of the plant material, removing the solvent and recovering (A). Alternatively the plant material is pressed to separate sap from solid plant material and the sap is used to obtain (A). Extract (A) is also claimed, and specifically contains 3-O-(beta -D-thevetopyranosyl-(1-4)- beta -D-cymaropyranosyl-(1-4)- beta -cymaropyranosyl)-12 beta -O-tigloyl-14 beta -hydroxy-pregn-4-en-20-one of formula (Ia). Steroid compounds of formula (I), i.e. (Ia) and various analogues, are new. R = alkyl; R1 = H, alkyl, tigloyl, benzoyl or other organic ester group; R2 = H; or one or more of 6-deoxy carbohydrates, 2,5-dideoxy carbohydrates and/or glucose molecules; broken lines indicate the optional presence of a further bond between C4-C5 or C5-C6. Also claimed are: (a) several further new analogues of (Ia); (b) a composition having appetite suppressant activity which contains a **melanocortin** 4 receptor **agonist**; (c) several processes for preparing compounds (I) and their intermediates; and (d) several novel steroid and mono-, di- and tri-saccharide intermediates.

USE - (A), (Ia), (I) and the other analogues of (Ia) and **melanocortin** 4 receptor **agonists** (including, but not restricted to, (A), (Ia) and the new analogues) are used to suppress appetite and/or to combat obesity in humans or animals. They are used in pharmaceutical compositions or in foodstuffs or beverages (all claimed).

ADVANTAGE - (A), (Ia) and the new analogues have strong appetite suppressant activity. Modified synthetic analogues of (Ia) can be prepared from progesterone, and may have improved binding to receptors and thus increased biological activity.

Dwg.0/6

L228 ANSWER 64 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1998-321582 [28] WPIDS
CROSS REFERENCE:. 1999-152890 [13]
DOC. NO. CPI: C1998-098874
TITLE: New quinazoline derivatives are **cholecystokinin** receptor **agonists** - useful for e.g. **suppressing appetite**, reducing gastric acid secretion, the treatment of anxiety, gastrointestinal ulcers and psychosis.
DERWENT CLASS: B02
INVENTOR(S): PADIA, J K

PATENT ASSIGNEE(S): (WARN) WARNER LAMBERT CO
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5756502	A	19980526	(199828)*		22

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 5756502	A	CIP of	US 1994-287454	19940808
			US 1995-500436	19950710

PRIORITY APPLN. INFO: US 1995-500436 19950710; US 1994-287454 19940808

AB US 5756502 A UPAB: 19990331
Quinazolinone derivatives of formula (I) are new. W-Z = CR3, CR4, CR5, CR6 or N, provided that not more than 2 of W-Z are N; R3-R6 = H, OH, sulphydryl, 1-4C alkoxy, 1-4C thioalkoxy, 1-4C alkyl, halo, CN, CF3, NO2, CO2R7 or NR7R8; R7, R8 = H or 1-4C alkyl; M = O or S; B = a bond or (CH2)iC(R9)(R10)CH2(CH2)j; i, j = 0-1; R9, R10 = H, 1-4C alkyl or 1-4C alkoxy; A = N(R1)C(O)(CH2)n, C(O)N(R11)(CH2)n, C(O)O(CH2)n, N(R11)S(O)2(CH2)n, N(R11)C(O)N(R12)(CH2)n, N(R11)C(O)N(R12)(CH2)n (sic), N(R11)C(=NH)N(R12)(CH2)n, N(R11)C(=NCN)N(R12)(CH2)n, N(R11)C(=NNO2)O(CH2)n, N(R11)C(=NH)O(CH2)n, N(R11)C(=NCH3)N(R12)(CH2)n, N(R11)C(=NNO2)N(R12)(CH2)n, N(R11)C(O)N(R12)S(O)2(CH2)n, N(R11)C(S)(CH2)n, N(R11)S(O)2N(R12)(CH2)n, N(R11)C(S)N(R12)S(O)2(CH2)n, OS(O)2N(R11)(CH2)n, OC(O)(CH2)n, OC(O)O(CH2)n, OC(S)(CH2)n or O(CH2)n; R11, R12 = H or 1-4C alkyl; n - 0-1; R1 = 1-6C alkyl, or phenyl, polyaromatic, heteroaromatic containing N, O and/or S, cyclo or polycycloalkyl hydrocarbyl, or mono or polyheterocyclyl containing 1-4 N, S and/or O, all optionally substituted by at least 1 of methyl, methoxy, F, Br, Cl, I, CF3, CN, acetyl, carboxy, carbmethoxy, carbethoxy, amino, N,N-dimethylamino, amido, acetyl (sic), methylene carboxy, tetrazolyl, NO2, cyclohexyl or adamantyl; and R2 = 1-6C alkyl, mono or polyheterocyclyl containing 1-4 N, S and/or O, or phenyl, polyaromatic, heteroaromatic containing N, O and/or S, or cyclo or polycycloalkyl hydrocarbyl, optionally substituted by at least 1 of methyl, methoxy, F, Cl, Br, I, OH, ethoxy, propoxy, i-propoxy, t-butoxy, ethyl, propyl, i-propyl, CF3, cyclopropoxy, thioisopropyl, CN, N,N-dimethylamino, N,N-dimethylaminomethyl, carboxy, carbmethoxy or tetrazolyl.

USE - (I) are used in compositions, in a unit dosage form, as appetite suppressants, gastric acid secretion reducing agents, anxiety reducing agents, gastrointestinal ulcer treating agents, psychosis treating agents, withdrawal reaction blocking agents, pain treatment agents, as agents for the treatment and prevention of panic and as agents for treating gastrin-dependent tumours (all claimed). (I) have good binding affinity for the central cholecystokinin A (CCK-A) and B (CCK-B) receptors. (I) can also be used as diagnostic tools for gastrin dependent tumours, by using radio labelled iodo derivatives of (I).
Dwg.0/0

L228 ANSWER 65 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1997-535361 [49] WPIDS
DOC. NO. CPI: C1997-171070
TITLE: Using glucagon-like peptide(s) for **appetite suppression** and satiety induction - specifically by administering glucagon-like peptide-2, or its derivatives with **glucagon-like peptide-1**; used to treat and/or prevent

obesity and type II diabetes.
DERWENT CLASS: B04 D16
INVENTOR(S): HOLST, J J; JUDGE, M E; MADSEN, O D; THIM, L; WULFF, B S; WUFF, B S; WULFF, B; DRAGSBAEK, O
PATENT ASSIGNEE(S): (NOVO) NOVO-NORDISK AS; (NOVO) NOVO NORDISK AS
COUNTRY COUNT: 76
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9731943	A1	19970904	(199749)*	EN	35
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN					
AU 9718715	A	19970916	(199803)		
NO 9804005	A	19980831	(199850)		
CZ 9802736	A3	19981216	(199904)		
EP 891378	A1	19990120	(199908)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LV NL PT RO SE SI					
US 5912229	A	19990615	(199930)		
CN 1215405	A	19990428	(199935)		
BR 9707807	A	19990727	(199941)		
AU 710818	B	19990930	(199952)		
HU 9902670	A2	20000128	(200015)		
JP 2000505460	W	20000509	(200032)		35
MX 9807086	A1	19990101	(200051)		
KR 99087439	A	19991227	(200059)		
EP 1231218	A2	20020814	(200261)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LV NL PT RO SE SI					
EP 891378	B1	20021113	(200282)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LV NL PT RO SE SI					
DE 69717092	E	20021219	(200307)		
RU 2197261	C2	20030127	(200321)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9731943	A1		WO 1997-DK86	19970227
AU 9718715	A		AU 1997-18715	19970227
NO 9804005	A		WO 1997-DK86	19970227
			NO 1998-4005	19980831
CZ 9802736	A3		WO 1997-DK86	19970227
			CZ 1998-2736	19970227
EP 891378	A1		EP 1997-905000	19970227
			WO 1997-DK86	19970227
US 5912229	A	Provisional	US 1996-15403P	19960315
		Provisional	US 1996-18865P	19960315
			US 1997-808825	19970228
CN 1215405	A		CN 1997-193525	19970227
BR 9707807	A		BR 1997-7807	19970227
			WO 1997-DK86	19970227
AU 710818	B		AU 1997-18715	19970227
HU 9902670	A2		WO 1997-DK86	19970227
			HU 1999-2670	19970227
JP 2000505460	W		JP 1997-530524	19970227
			WO 1997-DK86	19970227
MX 9807086	A1		MX 1998-7086	19980831
KR 99087439	A		WO 1997-DK86	19970227
			KR 1998-706861	19980901
EP 1231218	A2	Div ex	EP 1997-905000	19970227

			EP 2001-122701	19970227
EP 891378	B1		EP 1997-905000	19970227
			WO 1997-DK86	19970227
		Related to	EP 2001-122701	19970227
DE 69717092	E		DE 1997-617092	19970227
			EP 1997-905000	19970227
			WO 1997-DK86	19970227
RU 2197261	C2		WO 1997-DK86	19970227
			RU 1998-117915	19970227

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9718715	A	Based on	WO 9731943
CZ 9802736	A3	Based on	WO 9731943
EP 891378	A1	Based on	WO 9731943
BR 9707807	A	Based on	WO 9731943
AU 710818	B	Previous Publ.	AU 9718715
		Based on	WO 9731943
HU 9902670	A2	Based on	WO 9731943
JP 2000505460	W	Based on	WO 9731943
KR 99087439	A	Based on	WO 9731943
EP 1231218	A2	Div ex	EP 891378
EP 891378	B1	Related to	EP 1231218
		Based on	WO 9731943
DE 69717092	E	Based on	EP 891378
		Based on	WO 9731943
RU 2197261	C2	Based on	WO 9731943

PRIORITY APPLN. INFO: DK 1996-231 19960301; DK 1996-230 19960301

AB WO 9731943 A UPAB: 19971211

A claimed composition comprises a peptide of formula (I), given in one letter amino acid code, and an appetite-suppressing or satiety-inducing agent, preferably administered with glucagon-like peptide (GLP)-1.

X1HX2DGSFSDEMNTX3LDX4LAX5X6DFINWLX7X8TKITDX9 (I)

X1 = absent, DFPEEVAIVEELGRR, DFPEEVTIVEELGRR, or a fragment of these;

X2 = A or G;

X3 = I or V;

X4 = N, S or H;

X5 = A or T;

X6 = R or K;

X7 = I or L;

X8 = Q or H;

X9 = absent, K, R, RK, KR, RR or KK.

Also claimed is the use of a composition comprising a peptide of formula (I) for: (a) appetite suppression or satiety induction; and (b) prophylaxis and treatment of obesity or type II diabetes.

USE - Peptides of formula (I) are homologues or variants of glucagon-like peptide-2 (GLP-2) which has a powerful effect on inhibiting food intake when administered peripherally. It is thought that GLP-2 normally released from the intestinal L-cell together with GLP-1 also serves its own distinct role as a peripheral satiety factor. The peptides are used for the prevention and treatment of disorders associated with impaired appetite regulation, specifically obesity and type II diabetes.

Dwg.0/2

L228 ANSWER 66 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1997-051885 [05] WPIDS
DOC. NO. CPI: C1997-017163
TITLE: Compositions comprising amylin and

cholecystokinin agonists - useful for reducing food intake, **suppressing appetite** and controlling body weight.

DERWENT CLASS: B04 D16
INVENTOR(S): BEELEY, N R A; PRICKETT, K S; RINK, T J; YOUNG, A A; BEELEY, N R
PATENT ASSIGNEE(S): (AMYL-N) AMYLIN PHARM INC; (BEEL-I) BEELEY N R A; (PRIC-I) PRICKETT K S; (RINK-I) RINK T J; (YOUN-I) YOUNG A A
COUNTRY COUNT: 73
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9640196	A1	19961219	(199705)*	EN	66
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN					
AU 9659908	A	19961230	(199716)		
ZA 9604673	A	19970430	(199723)		69
US 5739106	A	19980414	(199822)		53
EP 844882	A1	19980603	(199826)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
JP 11507637	W	19990706	(199937)		54
MX 9709880	A1	19980301	(200002)		
CN 1192689	A	19980909	(200040)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9640196	A1	WO 1996-US9937	19960606
AU 9659908	A	AU 1996-59908	19960606
ZA 9604673	A	ZA 1996-4673	19960605
US 5739106	A	US 1995-477727	19950607
EP 844882	A1	EP 1996-917273	19960606
		WO 1996-US9937	19960606
JP 11507637	W	WO 1996-US9937	19960606
		JP 1997-502098	19960606
MX 9709880	A1	MX 1997-9880	19971208
CN 1192689	A	CN 1996-196092	19960606

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9659908	A	Based on	WO 9640196
EP 844882	A1	Based on	WO 9640196
JP 11507637	W	Based on	WO 9640196

PRIORITY APPLN. INFO: US 1995-477727 19950607

AB WO 9640196 A UPAB: 19970129
A compsn. comprising an amylin **agonist** and a **cholecystokinin** (CCK) **agonist** admixed in a form suitable for therapeutic administration is claimed. Also claimed are hybrid peptide compsns. comprising an amylin agonist peptide and a CCK agonist peptide covalently linked e.g. by the gp. -R1-R2-R3-R4-R5- where R1 = CONH(CH2)n, COO(CH2)n or CO(CH2)n; R2 = OCO(CH2)n, NHCO(CH2)n, OCOC6H4 (ortho, meta or para linked), COOC6H4 or NHCOC6H4 (both ortho, meta or para linked/substituted), CONHC6H4NH (ortho, meta or para substituted), O-X or NH-X; R3 = CH2, CF2, CO, CS or CNH; R4 = O or NH; R5 = (CH2)nNHCO,

(CH2)nOCO, (CH2)nCO; n = 1-6; and X = any amino acid linked via its carboxyl gp.

USE - The above compsns. can be used to reduce/suppress food intake, control appetite or control body weight in a mammal (claimed)

ADVANTAGE - Administration of amylin and CCK agonists in conjunction produces a greater effect than either administered alone; e.g. 0.1 mug/kg of each peptide causes a substantial reduction of food intake about equivalent to that seen with 100 mug/kg of either peptide alone.

Dwg.0/1

L228 ANSWER 67 OF 68 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1996-424683 [42] WPIDS
DOC. NO. CPI: C1996-133802
TITLE: New 4-phenyl-1,4-di hydro-3,5-pyridine-di carboxylic acid derivs. - useful as **neuropeptide Y antagonists**, esp. **anorectic** agents.
DERWENT CLASS: B02 B03
INVENTOR(S): BRUCE, M; JOHNSON, G; LEBOULLUEC, K; NOONAN, J W; POINDEXTER, G S; NOONON, J W
PATENT ASSIGNEE(S): (BRIM) BRISTOL-MYERS SQUIBB CO
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5554621	A	19960910	(199642)*		17
EP 747378	A1	19961211	(199703)	EN	25
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
AU 9654755	A	19961219	(199708)		
JP 09012572	A	19970114	(199712)		25
CA 2178414	A	19961208	(199715)		
AU 695882	B	19980827	(199846)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5554621	A	US 1995-482354	19950607
EP 747378	A1	EP 1996-109042	19960605
AU 9654755	A	AU 1996-54755	19960606
JP 09012572	A	JP 1996-145273	19960607
CA 2178414	A	CA 1996-2178414	19960606
AU 695882	B	AU 1996-54755	19960606

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 695882	B	Previous Publ.	AU 9654755

PRIORITY APPLN. INFO: US 1995-482354 19950607
AB US 5554621 A UPAB: 19961021

Neuropeptide Y (NPY) **antagonists** for promoting wt. loss and treating eating disorders (both claimed), and for treating hypertension, depression and anxiety, at doses of 0.05-1 mg/kg (parenteral) or 1-20 mg/kg (oral).

USE - (I) are useful as **neuropeptide Y** (NPY) **antagonists** for promoting wt. loss and treating eating disorders (claimed), and for treating hypertension, depression and anxiety, at doses of 0.05-1 mg/kg (parenteral) or 1-20 mg/kg (oral).

Dwg.0/0

L228 ANSWER 68 OF 68 WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER: 1995-051743 [07] WPIDS
DOC. NO. CPI: C1995-023671
TITLE: New **neuro peptide Y antagonists** and agonists - used to lower or increase blood pressure, to **suppress** or increase **appetite** or stimulate cardiovascular function.
DERWENT CLASS: B04
INVENTOR(S): BALASUBRAMANIAM, A
PATENT ASSIGNEE(S): (UYCI-N) UNIV CINCINNATI
COUNTRY COUNT: 48
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9500161	A1	19950105	(199507)*	EN	71
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB HU JP KP KR KZ LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US UZ VN					
AU 9471744	A	19950117	(199522)		
ZA 9404338	A	19950426	(199523)		70
EP 707490	A1	19960424	(199621)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
JP 11501281	W	19990202	(199915)		69

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9500161	A1	WO 1994-US6837	19940616
AU 9471744	A	AU 1994-71744	19940616
ZA 9404338	A	ZA 1994-4338	19940617
EP 707490	A1	EP 1994-920757	19940616
		WO 1994-US6837	19940616
JP 11501281	W	WO 1994-US6837	19940616
		JP 1995-502963	19940616

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9471744	A	Based on	WO 9500161
EP 707490	A1	Based on	WO 9500161
JP 11501281	W	Based on	WO 9500161

PRIORITY APPLN. INFO: US 1993-79319 19930618
AB WO 9500161 A UPAB: 19950223
Peptides of formulae (I)-(IV) and their salts are new: (R1)(R2)-A1-A2-A3-A4-A5-A6-Y-A25-A26-A27-A28-A29-A30-A31-A32-A33-A34-A35-A36-W (I) (R1)(R2)-X-A27-A28-A29-A30-A31-A32-A33-A34-A35-A36-W (II) (R1)(R2)-A1-A2-A3-A4-A5-A6-Y-A25-A26-A27'-A8-A9-Y'-A18-A19-A20-A21'-A22-A23-A24-A25-A26-A27-A28-A29-A30-A31-A32-A33-A34-A35-A36-W (III) (R1)(R2)-A18-A19-A20-A21-A22-A23-A24-A25-A26-A27-A28-A29-A30-A31-A32-A33-A34-A35-A36-W (IV) R1, R2 = H, 1-12C alkyl, 6-18C aryl, 1-12C acyl, 7-18C aralkyl or 7-18C alkaryl; A1 = Tyr or any aromatic amino acid; A2 = Pro, Hyp, D-Ala, N-Me-Ala, Ac6c, D-Pal or Asp; A3 = Ser, Thr, N-Me-Ser, N-Me-Thr, Ile, Val, Aib, Anb, Nle or N-Me-Leu; A4 = a D- or L-isomer selected from Lys, Arg, homo-Arg, diethyl-homo-Arg, Lys-epsilon-NH-R or Orn; R = H, 1-10C alkyl or 6-18C aryl; A5 = Pro, Hyp, D-Ala, N-Me-Ala, Ac6c, D-Pal or D-Trp; A6 = Gly or a D- or L-isomer selected from Asp, Glu, N-Me-Asp, Ala or Aoc; Y = A7-A8-A9-A10-A11-A12-A13-A14-A15-A16-A17-A18-A19-A20-A21-A22-A23-A24 or is absent; A7 = Asn, Ala, Gln, Gly or N-Me-Asn; A8 = Pro, Ser, Thr, Hyp, D-Ala, N-Me-Ala, Ac6c or D-Pal; A9 =

Gly, N-Me-Gly, Ala or Trp; A10 = Glu, Asp, N-Me-Glu, Ala or Nva; A11 = Asp. Glu, N-Me-Asp, Ala or Anb; A12 = Ala, Nal, Thi, Phe, Bth, Pcp or N-Me-Ala; A13 = Pro, Hyp, D-Ala, N-Me-Ala, Ac6c, D-Pal, Ser, Thr, N-Me-Ser, N-Me-Thr, Ala, Nal, Thi, Phe, Bth, Pcp, N-Me-Ala or Thr; A14 = Ala, Pro, Hyp, D-Ala, N-Me-Ala, Ac6c, D-Pal, Nal, Thi, Phe, Bth, Pcp or N-Me-Ala; A15 = Glu, Asp, N-Me-Glu, Ala or Nva; A16 = Asp, Glu, N-Me-Asp, Ala or Anb; A17 = Met, Leu, Ile, Val, Aib, Anb, Nle or N-Me-Leu; A18 = Ala, Asn, Gln, Gly, N-Me-Asn, Nal, Thi, Phe, Bth, Pcp or N-Me-Ala; A19 = a D- or L-isomer selected from Lys, Arg, homo-Arg, diethyl-homo-Arg, Lys-epsilon-NH-R or Orn; A20, A21 = as for A1; A22 = Ser, Thr, N-Me-Ser, N-Me-Thr, Ala, Nal, Thi, Phe, Bth, Pcp or N-Me-Ala; A23 = Ala, Ser, Thr, Nal, Thi, Phe, Bth, Pcp. N-Me-Ala, N-Me-Ser or N-Me-Thr; A24 = Leu, Ile, Val, Aib, Anb or N-Me-Leu; A25 = as for A4; A26 = as for A4 or a D- or L-isomer selected from His, Thr, 3-Me-His, beta-pyrazolylalanine or N-Me-His; A27 = a D- or L-isomer selected from any aromatic amino acid, Lys or a tethered amino acid with an indole ring; A28 = Aib or a D- or L-isomer selected from Ile, Leu, Val, Anb, Trp, N-Me-Ile or is absent; A29 = Asn, Ala, Gln, Gly, N-Me-Asn or is absent; A30 = Leu, Ile, Val, Aib, Anb or N-Me-Leu; A31 = Ile, Cys, Leu, Val, Aib, Anb or N-Me-Ile; A32 = a D- or L-isomer selected from any aromatic amino acid except L-Tyr, a tethered ami

Dwg.0/12

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=> fil capl;  d que 151; d que 153; d que 154
FILE 'CAPLUS' ENTERED AT 11:33:18 ON 12 JUN 2003
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FILE COVERS 1907 - 12 Jun 2003  VOL 138 ISS 24
FILE LAST UPDATED: 11 Jun 2003  (20030611/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L8         12265 SEA FILE=CAPLUS ABB=ON  ANTIDIABETIC AGENTS+OLD/CT
L9         48785 SEA FILE=CAPLUS ABB=ON  DIABETES MELLITUS/CT
L19          517 SEA FILE=CAPLUS ABB=ON  (MELANIN OR MELANOPHORE OR MELANOSOME)(
                 W)CONCENTRATING/OBI
L26        42315 SEA FILE=CAPLUS ABB=ON  AGONIST#/OBI
L30           12 SEA FILE=CAPLUS ABB=ON  L19(L)L26
L51            2 SEA FILE=CAPLUS ABB=ON  (L8 OR L9) AND L30



L8         12265 SEA FILE=CAPLUS ABB=ON  ANTIDIABETIC AGENTS+OLD/CT
L9         48785 SEA FILE=CAPLUS ABB=ON  DIABETES MELLITUS/CT
L21          143 SEA FILE=CAPLUS ABB=ON  (PROCOLIPASE OR ENTEROSTATIN)/OBI
L26        42315 SEA FILE=CAPLUS ABB=ON  AGONIST#/OBI
L32            2 SEA FILE=CAPLUS ABB=ON  L21(L)L26
L53            2 SEA FILE=CAPLUS ABB=ON  (L8 OR L9) AND L32



L4             1 SEA FILE=REGISTRY ABB=ON  LEPTIN/CN
L5           117 SEA FILE=REGISTRY ABB=ON  GLUCAGON-LIKE PEPTIDE 1?/CN
L6             1 SEA FILE=REGISTRY ABB=ON  "CORTICOTROPIN RELEASING FACTOR
                 (HUMAN)"/CN
L8         12265 SEA FILE=CAPLUS ABB=ON  ANTIDIABETIC AGENTS+OLD/CT
L9         48785 SEA FILE=CAPLUS ABB=ON  DIABETES MELLITUS/CT
L12         5857 SEA FILE=CAPLUS ABB=ON  L4 OR LEPTIN#/OBI
L13         1237 SEA FILE=CAPLUS ABB=ON  L5 OR GLUCAGON LIKE PEPTIDE(W)(I OR
                 1)/OBI
L14         5850 SEA FILE=CAPLUS ABB=ON  L6 OR CORTICOTROPIN RELEASING/OBI
L15         6847 SEA FILE=CAPLUS ABB=ON  NEUROPEPTIDE Y/OBI
L16         9872 SEA FILE=CAPLUS ABB=ON  CHOLECYSTOKININ/OBI
L17         2120 SEA FILE=CAPLUS ABB=ON  GALANIN/OBI
L20         1030 SEA FILE=CAPLUS ABB=ON  MELANOCORTIN/OBI
L25       806180 SEA FILE=CAPLUS ABB=ON  ANTAGONIST#/OBI OR INHIBIT?/OBI
L26        42315 SEA FILE=CAPLUS ABB=ON  AGONIST#/OBI
L27          925 SEA FILE=CAPLUS ABB=ON  L15(L)L25
L28          302 SEA FILE=CAPLUS ABB=ON  L16(L)L26
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L29          322 SEA FILE=CAPLUS ABB=ON  L17(L)L25
L31          141 SEA FILE=CAPLUS ABB=ON  L20(L)L26
L54            2 SEA FILE=CAPLUS ABB=ON  (L8 OR L9) AND L12 AND L13 AND L14 AND
                 L27 AND L28 AND L29 AND L31

=> s (l51 or l53 or l54) not l224

L229           2 (L51 OR L53 OR L54) NOT L224

=> fil medl

FILE 'MEDLINE' ENTERED AT 11:33:19 ON 12 JUN 2003

  FILE LAST UPDATED: 11 JUN 2003 (20030611/UP). FILE COVERS 1958 TO DATE.

  On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

  MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
  MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
  for a description on changes.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> d que l90; d que l91; d que l92; d que l97

L58          149 SEA FILE=MEDLINE ABB=ON  NEUROPEPTIDE Y/CT(L)AI/CT
L59           31 SEA FILE=MEDLINE ABB=ON  CHOLECYSTOKININ+NT/CT(L)AG/CT
L60           10 SEA FILE=MEDLINE ABB=ON  GLUCAGON/CT(L)AG/CT
L63           39 SEA FILE=MEDLINE ABB=ON  GALANIN/CT(L)AI/CT
L64          436 SEA FILE=MEDLINE ABB=ON  (MELANIN OR MELANOPHORE OR MELANOSOME)
                 (W)CONCENTRATING(W)HORMONE#
L65            1 SEA FILE=MEDLINE ABB=ON  (PROCOLIPASE OR ENTEROSTATIN)(3A)AGONI
                 ST#
L66            1 SEA FILE=MEDLINE ABB=ON  TRIPEPTIDYLPEPTIDASE(W)(II OR
                 2)(3A)(ANTAGONI? OR INHIBIT?)
L82        12290 SEA FILE=MEDLINE ABB=ON  HYPOGLYCEMIC AGENTS/CT
L83        16344 SEA FILE=MEDLINE ABB=ON  DIABETES MELLITUS/CT(L)TH./CT
L90            4 SEA FILE=MEDLINE ABB=ON  (L82 OR L83) AND (L59 OR L60 OR L63
                 OR L65 OR L66 OR L58 OR L64)


L57         5092 SEA FILE=MEDLINE ABB=ON  LEPTIN/CT
L62         1301 SEA FILE=MEDLINE ABB=ON  GLUCAGON LIKE PEPTIDE(W)(1 OR I)
L82        12290 SEA FILE=MEDLINE ABB=ON  HYPOGLYCEMIC AGENTS/CT
L83        16344 SEA FILE=MEDLINE ABB=ON  DIABETES MELLITUS/CT(L)TH./CT
L91            1 SEA FILE=MEDLINE ABB=ON  (L82 OR L83) AND (L62 AND L57)


L57         5092 SEA FILE=MEDLINE ABB=ON  LEPTIN/CT
L61         7135 SEA FILE=MEDLINE ABB=ON  CORTICOTROPIN-RELEASING HORMONE/CT
L62         1301 SEA FILE=MEDLINE ABB=ON  GLUCAGON LIKE PEPTIDE(W)(1 OR I)
L82        12290 SEA FILE=MEDLINE ABB=ON  HYPOGLYCEMIC AGENTS/CT
L83        16344 SEA FILE=MEDLINE ABB=ON  DIABETES MELLITUS/CT(L)TH./CT
L92            1 SEA FILE=MEDLINE ABB=ON  (L82 OR L83) AND (L62 OR L57) AND L61


L61         7135 SEA FILE=MEDLINE ABB=ON  CORTICOTROPIN-RELEASING HORMONE/CT
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previously printed

TH = therapy

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L82        12290 SEA FILE=MEDLINE ABB=ON  HYPOGLYCEMIC AGENTS/CT
L83        16344 SEA FILE=MEDLINE ABB=ON  DIABETES MELLITUS/CT(L)TH./CT
L97            2 SEA FILE=MEDLINE ABB=ON  (L82/MAJ OR L83/MAJ) AND L61


=> s (l90 or l91 or l92 or l97) not l225

L230           8 (L90 OR L91 OR L92 OR L97) NOT L225

=> fil embase

FILE 'EMBASE' ENTERED AT 11:33:21 ON 12 JUN 2003
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 FILE COVERS 1974 TO 5 Jun 2003 (20030605/ED)

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 substance identification.

=> d que l180;d que l183; d que l186

L104           3 SEA FILE=EMBASE ABB=ON  LEPTIN RESISTANCE/CT
L106         256 SEA FILE=EMBASE ABB=ON  CHOLECYSTOKININ RECEPTOR STIMULATING
                 AGENT/CT
L112         350 SEA FILE=EMBASE ABB=ON  MELANOCORTIN/CT
L113          93 SEA FILE=EMBASE ABB=ON  ENTEROSTATIN/CT
L155      146621 SEA FILE=EMBASE ABB=ON  DIABETES MELLITUS+NT/CT
L156        5103 SEA FILE=EMBASE ABB=ON  ANTIDIABETIC AGENT/CT
L157       22496 SEA FILE=EMBASE ABB=ON  L155(L)(DT OR PC)/CT
L161       20745 SEA FILE=EMBASE ABB=ON  L156/MAJ OR L157/MAJ
L180           6 SEA FILE=EMBASE ABB=ON  L161 AND (L104 OR L106 OR L112 OR
                 L113)



L102           2 SEA FILE=EMBASE ABB=ON  LEPTIN RECEPTOR AGONIST/CT
L105          11 SEA FILE=EMBASE ABB=ON  NEUROPEPTIDE Y ANTAGONIST/CT
L108           2 SEA FILE=EMBASE ABB=ON  GLUCAGON LIKE PEPTIDE 1 AGONIST/CT
L110         379 SEA FILE=EMBASE ABB=ON  MELANIN CONCENTRATING HORMONE/CT
L111           1 SEA FILE=EMBASE ABB=ON  MELANOCORTIN AGONIST/CT
L114           1 SEA FILE=EMBASE ABB=ON  ENTEROSTATIN RECEPTOR AGONIST/CT
L115           1 SEA FILE=EMBASE ABB=ON  TRIPEPTIDYLPEPTIDASE/CT
L155      146621 SEA FILE=EMBASE ABB=ON  DIABETES MELLITUS+NT/CT
L156        5103 SEA FILE=EMBASE ABB=ON  ANTIDIABETIC AGENT/CT
L157       22496 SEA FILE=EMBASE ABB=ON  L155(L)(DT OR PC)/CT
L183           0 SEA FILE=EMBASE ABB=ON  (L156 OR L157) AND (L102 OR L105 OR
                 L108 OR L110 OR L111 OR (L114 OR L115))



L101        5382 SEA FILE=EMBASE ABB=ON  LEPTIN/CT
L103         813 SEA FILE=EMBASE ABB=ON  LEPTIN RECEPTOR/CT
L107         967 SEA FILE=EMBASE ABB=ON  GLUCAGON LIKE PEPTIDE 1/CT
L109       19375 SEA FILE=EMBASE ABB=ON  GLUCAGON/CT
L116        7676 SEA FILE=EMBASE ABB=ON  CORTICOTROPIN RELEASING FACTOR/CT
L155      146621 SEA FILE=EMBASE ABB=ON  DIABETES MELLITUS+NT/CT
L156        5103 SEA FILE=EMBASE ABB=ON  ANTIDIABETIC AGENT/CT
L157       22496 SEA FILE=EMBASE ABB=ON  L155(L)(DT OR PC)/CT
L161       20745 SEA FILE=EMBASE ABB=ON  L156/MAJ OR L157/MAJ
L186           6 SEA FILE=EMBASE ABB=ON  (L103 OR L116) AND L161 AND (L101 OR
                 L107 OR L109)
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=> s (l180 or l186) not l226

L231 10 (L180 OR L186) NOT (L226) previously printed

=> dup rem l230,l229,l231
FILE 'MEDLINE' ENTERED AT 11:33:41 ON 12 JUN 2003

FILE 'CAPLUS' ENTERED AT 11:33:41 ON 12 JUN 2003
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FILE 'EMBASE' ENTERED AT 11:33:41 ON 12 JUN 2003

PROCESSING COMPLETED FOR L230
PROCESSING COMPLETED FOR L229
PROCESSING COMPLETED FOR L231
L232 20 DUP REM L230 L229 L231 (0 DUPLICATES REMOVED)
ANSWERS '1-8' FROM FILE MEDLINE
ANSWERS '9-10' FROM FILE CAPLUS
ANSWERS '11-20' FROM FILE EMBASE

=> d ibib ab hitrn 1-20; fil hom

L232 ANSWER 1 OF 20 MEDLINE
ACCESSION NUMBER: 2003094689 MEDLINE
DOCUMENT NUMBER: 22494537 PubMed ID: 12606517
TITLE: Development and characterization of a glucagon-like peptide 1-albumin conjugate: the ability to activate the glucagon-like peptide 1 receptor in vivo.
AUTHOR: Kim Jung-Guk; Baggio Laurie L; Bridon Dominique P; Castaigne Jean-Paul; Robitaille Martin F; Jette Lucie; Benquet Corinne; Drucker Daniel J
CORPORATE SOURCE: Banting and Best Diabetes Centre, Department of Medicine, University of Toronto, Toronto General Hospital, 200 Elizabeth Street, Toronto, Ontario, Canada M5G 2C4.
SOURCE: DIABETES, (2003 Mar) 52 (3) 751-9.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030228
Last Updated on STN: 20030513
Entered Medline: 20030509

AB The rapid degradation of native glucagon-like peptide 1 (GLP-1) by dipeptidyl peptidase-IV (DPP-IV) has fostered new approaches for generation of degradation-resistant GLP-1 analogues. We examined the biological activity of CJC-1131, a DPP-IV-resistant drug affinity complex (DAC) GLP-1 compound that conjugates to albumin in vivo. The CJC-1131 albumin conjugate bound to the GLP-1 receptor (GLP-1R) and activated cAMP formation in heterologous fibroblasts expressing a GLP-1R. CJC-1131 lowered glucose in wild-type mice, but not in GLP-1R-/- mice. Basal glucose and glycemic excursion following glucose challenge remained significantly reduced 10-12 h following a single injection of CJC-1131. Twice daily administration of CJC-1131 to db/db mice significantly reduced glycemic excursion following oral and IP glucose challenge ($P < 0.01$ to 0.05) but did not significantly lower body weight during the 4-week study period. Levels of random fed glucose were significantly lower in CJC-1131-treated +/+ and db/db mice and remained significantly lower even

1 week following discontinuation of CJC-1131 administration. CJC-1131 increased levels of pancreatic proinsulin mRNA transcripts, percent islet area, and the number of bromodeoxyuridine-positive islet cells. These findings demonstrate that an albumin-conjugated DAC:GLP-1 mimics the action of native GLP-1 and represents a new approach for prolonged activation of GLP-1R signaling.

L232 ANSWER 2 OF 20 MEDLINE
ACCESSION NUMBER: 2002698613 MEDLINE
DOCUMENT NUMBER: 22316411 PubMed ID: 12429558
TITLE: Intraventricular insulin potentiates the anorexic effect of corticotropin releasing hormone in rats.
AUTHOR: Richardson Ralph D; Omachi Koichi; Kermani Rasoul; Woods Stephen C
CORPORATE SOURCE: Veterans Affairs Puget Sound Health Care System, Seattle 98108, USA.
CONTRACT NUMBER: DK-17844 (NIDDK)
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY. REGULATORY, INTEGRATIVE AND COMPARATIVE PHYSIOLOGY, (2002 Dec) 283 (6) R1321-6. Journal code: 100901230. ISSN: 0363-6119.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20021219
Entered Medline: 20021218

AB Intraventricular corticotropin releasing hormone (CRH) suppresses food intake and body weight as a stress response. Insulin, acting within the brain, also suppresses food intake and body weight, and this suppression is related to caloric homeostasis. We determined if increased insulin within the brain potentiates the anorexic effects of intraventricular CRH. Rats were food deprived for 17 h each day and then given 30-min access to Ensure. One-half received continuous third ventricular infusion of synthetic cerebrospinal fluid via osmotic minipumps, and one-half received insulin (0.6 mU/day). During the infusion, rats also received 0, 0.1, 1.0, or 5.0 microg of CRH into the lateral ventricle just before access to Ensure. Insulin alone had no effect on Ensure intake or body weight. CRH dose dependently reduced Ensure intake in both groups, and the reduction was greater in the insulin group. Hence, central insulin potentiated the ability of centrally administered CRH to suppress food intake. These findings suggest that stress-related influences over food intake, particularly those mediated via CRH, interact with relative adiposity as signaled to the brain by central insulin.

L232 ANSWER 3 OF 20 MEDLINE
ACCESSION NUMBER: 2002498932 MEDLINE
DOCUMENT NUMBER: 22178239 PubMed ID: 12191802
TITLE: Does neuropeptide Y contribute to the modulation of brain stimulation reward by chronic food restriction?.
AUTHOR: Fulton Stephanie; Woodside Barbara; Shizgal Peter
CORPORATE SOURCE: Center for Studies in Behavioural Neurobiology, Concordia University, Hall Building Rm-1013, 1455 de Maisonneuve Blvd, Montreal QC, Canada H3G 1M8.
SOURCE: BEHAVIOURAL BRAIN RESEARCH, (2002 Aug 21) 134 (1-2) 157-64. Journal code: 8004872. ISSN: 0166-4328.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 20021004

Last Updated on STN: 20021213
Entered Medline: 20021119

AB The rewarding effect produced by electrically stimulating particular sites in the lateral hypothalamus (LH) can be enhanced by chronic food restriction and body weight loss. The impact on brain stimulation reward (BSR) of certain hormones involved in the regulation of energy balance, such as leptin and corticotropin-releasing hormone, depends upon the sensitivity of BSR to food restriction. The present investigation assessed the influence of neuropeptide Y (NPY), a potent orexigenic peptide, on BSR generated by stimulating restriction-sensitive and -insensitive sites in the LH. Twelve male Long Evans rats were trained to press a lever for a rewarding train of stimulation. Rate-frequency curves, reflecting the number of rewards earned as a function of the stimulation frequency, were collected during free-feeding and then again following a period of food restriction and 20-25% body weight loss. NPY (4 microg) was administered intraventricularly during the food restriction condition. Alterations in the rewarding effect of the stimulation were assessed by measuring changes in the frequency required to maintain half-maximal rewards earned (M-50). In half of the subjects, food restriction produced significant decreases in M-50 values, indicating that the reward effectiveness of the stimulation was potentiated. In contrast, M-50 values were unaltered by food restriction in the remaining six animals. In most of the subjects in which M-50 values decreased following chronic food restriction, NPY failed to alter BSR. Similarly, BSR was unchanged by NPY administration in most of the rats with restriction-insensitive stimulation sites. These findings suggest that NPY does not take part in the process whereby food restriction and leptin modulate reward circuitry activated by stimulating restriction-sensitive sites.

L232 ANSWER 4 OF 20 MEDLINE
ACCESSION NUMBER: 2002714950 MEDLINE
DOCUMENT NUMBER: 22364877 PubMed ID: 12477297
TITLE: Novel peptides under development for the treatment of type 1 and type 2 diabetes mellitus.
AUTHOR: Baron Alain D; Kim Dennis; Weyer Christian
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., 9373 Towne Centre Drive, Suite 250, San Diego, CA 92121, USA.. abaron@amylin.com
SOURCE: Curr Drug Targets Immune Endocr Metabol Disord, (2002 Apr) 2 (1) 63-82. Ref: 169
Journal code: 101121150. ISSN: 1568-0088.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030129
Entered Medline: 20030128

AB Recent availability of expanded treatment options for both type 1 and type 2 diabetes has not translated into easier and significantly better glycemic and metabolic management. Patients with type 1 diabetes continue to experience increased risk of hypoglycemic episodes and progressive weight gain resulting from intensive insulin treatment, despite the recent availability of a variety of insulin analog. Given the progressive nature of the disease, most patients with type 2 diabetes inevitably proceed from oral agent monotherapy to combination therapy and, ultimately, require exogenous insulin replacement. Insulin therapy in type 2 diabetes is also accompanied by untoward weight gain. Both type 1 and type 2 diabetes continue to be characterized by marked postprandial hyperglycemia. Two

hormones still in development are candidates for pharmacologic intervention, have novel modes of action (some centrally mediated), and show great promise in addressing some of the unmet needs of current diabetes management. Pramlintide acetate, an analog of the beta cell hormone amylin and the first non-insulin related therapeutic modality for type 1 and type 2 diabetic patients with severe beta cell failure, may be useful as adjunctive therapy to insulin. The principal anti-diabetic effects of pramlintide arise from interactions via its cognate receptors located in the central nervous system resulting in postprandial glucagon suppression, modulation of nutrient absorption rate, and reduction of food intake. Another polypeptide hormone, exendin-4, exerts at least some of its pharmacologic actions as an agonist at the glucagon-like peptide-1 (GLP-1) receptor. GLP-1 and related compounds exhibit multiple modes of action, the most notable being a glucose-dependent insulinotropic effects and the potential to preserve or improve the beta-cell function. The latter effect could potentially halt or delay the progressive deterioration of the diabetic state associated with type 2 diabetes. Physiologically, both amylin and glucagon-like peptide (GLP)-1, along with insulin, are involved in a coordinated and concerted interplay between hormones acting both centrally and peripherally to provide meticulous control over the rate of appearance of exogenous and endogenous glucose and to match that rate to the rate of glucose disappearance. Both hormones are deficient in diabetes. Therapies directed at restoring this complex physiology have the potential to facilitate glucose control and thus minimize the attendant complications of diabetes.

L232 ANSWER 5 OF 20 MEDLINE
ACCESSION NUMBER: 2001560502 MEDLINE
DOCUMENT NUMBER: 21518482 PubMed ID: 11606455
TITLE: Molecular regulation of the hypothalamo-pituitary-adrenal axis in streptozotocin-induced diabetes: effects of insulin treatment.
AUTHOR: Chan O; Chan S; Inouye K; Vranic M; Matthews S G
CORPORATE SOURCE: Department of Physiology, University of Toronto, Toronto, Ontario, Canada M5S 1A8.
SOURCE: ENDOCRINOLOGY, (2001 Nov) 142 (11) 4872-9.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011022
Last Updated on STN: 20020122
Entered Medline: 20011204

AB Increased hypothalamo-pituitary-adrenocortical (HPA) activity in diabetes is likely important in the development of some pathologies associated with the disorder. We hypothesized that central regulation of HPA activity differs among normal, streptozotocin (STZ)-diabetic, and insulin-treated diabetic rats. Blood glucose, ACTH, and corticosterone were elevated, 8 d after inducing diabetes. Insulin treatment normalized these parameters. Plasma norepinephrine was similar in all groups, but epinephrine was lower in STZ-diabetic and higher in insulin-treated rats vs. normals. Increased ACTH with diabetes corresponded with increased hypothalamic CRH mRNA, but no change in pituitary POMC mRNA. With insulin-treatment, CRH mRNA remained elevated, and POMC mRNA was unaltered. Hippocampal MR mRNA expression was dramatically increased with diabetes and, moreover, was not normalized by insulin. No differences in GR mRNA were detected between normal and STZ-diabetic rats. However, insulin treatment increased GR mRNA levels in the paraventricular nucleus and pituitary. We postulate that, in STZ-diabetes: 1) increased HPA activity is caused by increased central drive at and/or above the level of the paraventricular nucleus and is associated with decreased epinephrine; and 2) normalized

pituitary-adrenal activity with insulin may be caused by the compensatory increase in GR mRNA allowing glucocorticoid-mediated suppression of ACTH secretion despite the residual increase in central HPA activity. Thus, insulin apparently restored HPA activity at and below the pituitary but, surprisingly, not above it.

L232 ANSWER 6 OF 20 MEDLINE
ACCESSION NUMBER: 2001197457 MEDLINE
DOCUMENT NUMBER: 21183108 PubMed ID: 11289473
TITLE: Effect of metformin on **glucagon-like peptide 1** (GLP-1) and leptin levels in obese nondiabetic subjects.
COMMENT: Comment in: Diabetes Care. 2002 Aug;25(8):1490-1; author reply 1491-2
AUTHOR: Mannucci E; Ognibene A; Cremasco F; Bardini G; Mencucci A; Pierazzuoli E; Ciani S; Messeri G; Rotella C M
CORPORATE SOURCE: Department of Clinical Pathophysiology, University of Florence, Italy.
SOURCE: DIABETES CARE, (2001 Mar) 24 (3) 489-94.
Journal code: 7805975. ISSN: 0149-5992.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20030114
Entered Medline: 20010614

AB OBJECTIVE: To evaluate the effects of metformin on **glucagon-like peptide 1** (GLP-1) and leptin levels.
RESEARCH DESIGN AND METHODS: A total of 10 obese nondiabetic male patients were studied before and after a 14-day treatment with 2,550 mg/day metformin and were compared with 10 untreated obese control subjects. On days 0 and 15, leptin and GLP-1(7-36)amide/(7-37) levels were assessed before and after an oral glucose load during a euglycemic hyperinsulinemic clamp to avoid the interference of variations of insulinemia and glycemia on GLP-1 and leptin secretion. The effects of metformin on GLP-1(7-36)amide degradation in human plasma and in a buffer solution containing dipeptidyl peptidase IV (DPP-IV) were also studied. RESULTS: Leptin levels were not affected by the oral glucose load, and they were not modified after metformin treatment. Metformin induced a significant ($P < 0.05$) increase of GLP-1(7-36)amide/(7-37) at 30 and 60 min after the oral glucose load (63.8 +/- 29.0 vs. 50.3 +/- 15.6 pmol/l and 75.8 +/- 35.4 vs. 46.9 +/- 20.0 pmol/l, respectively), without affecting baseline GLP-1 levels. No variations of GLP-1 levels were observed in the control group. In pooled human plasma, metformin (0.1-0.5 microg/ml) significantly inhibited degradation of GLP-1(7-36)amide after a 30-min incubation at 37 degrees C; similar results were obtained in a buffer solution containing DPP-IV. CONCLUSIONS: Metformin significantly increases GLP-1 levels after an oral glucose load in obese nondiabetic subjects; this effect could be due to an inhibition of GLP-1 degradation.

L232 ANSWER 7 OF 20 MEDLINE
ACCESSION NUMBER: 2001034561 MEDLINE
DOCUMENT NUMBER: 20414334 PubMed ID: 10959776
TITLE: New approaches in the treatment of type 2 diabetes.
AUTHOR: Zhang B B; Moller D E
CORPORATE SOURCE: Department of Molecular Endocrinology, Merck Research Laboratories, Rahway, NJ 07065, USA.. bei_zhang@merck.com
SOURCE: CURRENT OPINION IN CHEMICAL BIOLOGY, (2000 Aug) 4 (4)

461-7. Ref: 50
Journal code: 9811312. ISSN: 1367-5931.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001130

AB Type 2 diabetes is a chronic metabolic derangement that results from defects in both insulin action and secretion. New thiazolidinedione insulin sensitizers have been recently launched. New approaches with mechanisms different from current therapies are being explored, including novel ligands of peroxisome proliferator-activated receptor, glucagon receptor antagonists, dipeptidyl peptidase IV inhibitors, and insulin receptor activators.

L232 ANSWER 8 OF 20 MEDLINE
ACCESSION NUMBER: 1999043799 MEDLINE
DOCUMENT NUMBER: 99043799 PubMed ID: 9824666
TITLE: Intra-septal injections of glucose and glibenclamide attenuate galanin-induced spontaneous alternation performance deficits in the rat.
AUTHOR: Stefani M R; Gold P E
CORPORATE SOURCE: Neuroscience Graduate Program and Department of Psychology, University of Virginia, Charlottesville, VA 22903, USA.
CONTRACT NUMBER: AG07648 (NIA)
NS32914 (NINDS)
SOURCE: BRAIN RESEARCH, (1998 Nov 30) 813 (1) 50-6.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 19990202
Last Updated on STN: 19990202
Entered Medline: 19990120

AB Injection of the neuroactive peptide galanin into the rat hippocampus and medial septal area impairs spatial memory and cholinergic system activity. Conversely, injection of glucose into these same brain regions enhances spatial memory and cholinergic system activity. Glucose and galanin may both modulate neuronal activity via opposing actions at ATP-sensitive K+ (K-ATP) channels. The experiments described in this report tested the ability of glucose and the direct K-ATP channel blocker glibenclamide to attenuate galanin-induced impairments in spontaneous alternation performance in the rat. Intra-septal injection of galanin (2.5 microgram), 30 min prior to plus-maze spontaneous alternation performance, significantly decreased alternation scores compared to those of rats receiving injections of vehicle solution. Co-injection of glucose (20 nmol) or the K-ATP channel blocker glibenclamide (5 nmol) attenuated the galanin-induced performance deficits. Glibenclamide produced an inverted-U dose-response curve in its interaction with galanin, with doses of 0.5 and 10 nmol having no effect on galanin-induced spontaneous alternation deficits. Drug treatments did not alter motor activity, as measured by overall number of arm entries during spontaneous alternation testing, relative to vehicle injected controls. These findings support the hypothesis that, in the septal region, galanin and glucose act via K-ATP channels to modulate neural function and behavior.

L232 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:314938 CAPLUS
DOCUMENT NUMBER: 136:340674
TITLE: Alpha-aryl ethanolamines and their use as beta-3 adrenergic receptor agonists, for treatment of diseases and disorders, for increasing lean meat content in animals, and for use in combination with other antiobesity agents
INVENTOR(S): Day, Robert Francis; Lafontaine, Jennifer Anne
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032897	A1	20020425	WO 2001-IB1847	20011004
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001092161	A5	20020429	AU 2001-92161	20011004
US 2002052392	A1	20020502	US 2001-981551	20011017
US 6566377	B2	20030520		

PRIORITY APPLN. INFO.: US 2000-242274P P 20001020
WO 2001-IB1847 W 20011004
OTHER SOURCE(S): MARPAT 136:340674
AB The invention provides .beta.3-adrenergic receptor agonists (no data) of structural formula I [wherein Ar = pyridyl, oxazolyl, thiazolyl, or Ph; R = H, OH, oxo, halo, CF3, alkyl, alkoxy, cycloalkyl, NH2 or certain derivs., sulfonyl groups; R1 = H, alkyl, halo, alkoxy, OH; R2, R3, R4 = H, alkyl; R5 = 5- or 6-membered heterocycle with 1-4 N/O/S atoms; R6, R7 = H, halo, cyano, oxo, acyl, CO2H or derivs., OH, NH2 or derivs., (un)substituted alkyl, etc.; R8 = H, alkyl, halo; X = direct bond or O; Y = direct bond, alkylene, OCH2, CH2O, or O; with provisos], as well as the stereoisomers and prodrugs thereof, and the pharmaceutically acceptable salts of the compds., stereoisomers, and prodrugs. The invention further provides intermediates useful in the prepn. of I, as well as therapeutic combinations of I and/or their stereoisomers/prodrugs/salts, with (other) anti-obesity agents. Over 60 invention compds. and 40 intermediates are named individually in claims. Exemplary prepns. of many intermediates and several invention compds. are given. For instance, reaction of (R)-2-chloro-5-oxiranylpyridine with 2-[4-(4-phenylthiazol-2-yl)phenoxy]ethylamine (prepn. given) in EtOH at 80.degree. gave 50% title compd. (R)-II.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L232 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:457194 CAPLUS
DOCUMENT NUMBER: 133:85156
TITLE: Human melanin concentrating hormone receptor MCH1 and cDNA and diagnostic and therapeutic uses thereof
INVENTOR(S): Salon, John A.; Laz, Thomas M.; Nagorny, Raisa;

Wilson, Amy E.
PATENT ASSIGNEE(S): Synaptic Pharmaceutical Corporation, USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039279	A2	20000706	WO 1999-US31169	19991230
WO 2000039279	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6221613	B1	20010424	US 1998-224426	19981231
CA 2358687	AA	20000706	CA 1999-2358687	19991230
EP 1141020	A2	20011010	EP 1999-969993	19991230
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533116	T2	20021008	JP 2000-591172	19991230
US 6221616	B1	20010424	US 2000-478601	20000106
US 6291195	B1	20010918	US 2000-478602	20000106
US 2002111306	A1	20020815	US 2001-885478	20010620
US 2003082623	A1	20030501	US 2001-899732	20010705
US 2003077701	A1	20030424	US 2001-29314	20011220

PRIORITY APPLN. INFO.:
US 1998-224426 A2 19981231
WO 1999-US31169 W 19991230
US 2000-610635 A2 20000705
US 2001-899732 A1 20010705

AB This invention provides an isolated nucleic acid encoding a human MCH1 receptor; a purified human MCH1 receptor; vectors comprising isolated nucleic acid encoding a human MCH1 receptor; cells comprising such vectors; antibodies directed to a human MCH1 receptor; nucleic acid probes useful for detecting nucleic acid encoding human MCH1 receptors; antisense oligonucleotides complementary to unique sequences of nucleic acid encoding human MCH1 receptors; transgenic, nonhuman animals which express DNA encoding a normal or mutant human MCH1 receptor; methods of isolating a human MCH1 receptor; methods of treating an abnormality that is linked to the activity of a human MCH1 receptor; and methods of detg. binding of compds. to mammalian MCH1 receptors. Thus, the cDNA for human MCH1 was cloned and sequenced. Treatment of recombinant COS-7 cells expressing human MCH1 with MCH resulted in stimulation of intracellular inositol phosphate release as well as stimulation of expression of a c-fos-regulated reporter gene. CHO cells producing MCH1 exhibited a dose-dependent increase in acidification rate when treated with MCH. MRNA encoding the human MCH1 was widespread throughout all tissues assayed, including both CNS and peripheral organs.

L232 ANSWER 11 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003193750 EMBASE
TITLE: Antiobesity and antidiabetic effects of brain-derived neurotrophic factor in rodent models of leptin resistance.
AUTHOR: Nakagawa T.; Ogawa Y.; Ebihara K.; Yamanaka M.; Tsuchida A.; Taiji M.; Noguchi H.; Nakao K.
CORPORATE SOURCE: Dr. Y. Ogawa, Dept. of Med. and Clinical Science, Kyoto

Univ. Grad. School of Medicine, 54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan. ogawa@kuhp.kyoto-u.ac.jp
SOURCE: International Journal of Obesity, (1 May 2003) 27/5 (557-565).
Refs: 43
ISSN: 0307-0565 CODEN: IJOBDP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB OBJECTIVE: Obesity in rodents and humans is mostly associated with elevated plasma leptin concentrations, suggesting a new pathological concept of 'leptin resistance'. We have demonstrated that brain-derived neurotrophic factor (BDNF) can improve obesity and diabetes of C57BL/KsJ db/db (db/db) mice. In this study, we investigated whether or not BDNF is effective in two different models of leptin resistance, an acquired model and a genetic model. DESIGN: C57BL/6J mice rendered obese by consumption of a high-fat diet (diet-induced obesity (DIO) mice) were used as an acquired model and lethal yellow ogouti mice (KKA(y) mice) as a genetic model of leptin resistance. Food intake and glucose metabolism were studied after acute or repetitive administration of BDNF. RESULTS: Intraperitoneal administration of BDNF (10 mg/kg, twice/day) significantly reduced cumulative food intake of DIO and KKA(y) mice, whereas they were unresponsive to leptin administration. Repetitive subcutaneous administration of BDNF (10 mg/kg daily for 6 days) reduced food intake and improved impaired glucose tolerance in DIO mice. Pair feeding of vehicle-treated DIO mice with the same amount of chow consumed by the BDNF-treated group did not improve the impaired glucose homeostasis, indicating that the antidiabetic effect is not due to decreased food intake. We also observed that BDNF is effective in improving obesity and diabetes of KKA(y) mice. CONCLUSION: This study demonstrated antiobesity and antidiabetic effects of BDNF in two different models of leptin resistance, thereby suggesting the therapeutic potential of BDNF in the treatment of leptin-resistant obesity and diabetes.

L232 ANSWER 12 OF 20 EMBASE
ACCESSION NUMBER: 2003189352 EMBASE
TITLE: A study to survey susceptible genetic factors responsible for troglitazone-associated hepatotoxicity in Japanese patients with type 2 diabetes mellitus.
AUTHOR: Watanabe I.; Tomita A.; Shimizu M.; Sugawara M.; Yasumo H.; Koishi R.; Takahashi T.; Miyoshi K.; Nakamura K.; Izumi T.; Matsushita Y.; Furukawa H.; Haruyama H.; Koga T.
CORPORATE SOURCE: Dr. T. Koga, Biomedical Research Laboratories, Sankyo Co., Ltd., 2-58 Hiromachi 1-chome, Shinagawa-ku, Tokyo 140-8710, Japan. kogasa@shina.sankyo.co.jp
SOURCE: Clinical Pharmacology and Therapeutics, (1 May 2003) 73/5 (435-455).
Refs: 38
ISSN: 0009-9236 CODEN: CLPTAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background and Objective: Troglitazone is a 2,4-thiazolidinedione antidiabetic agent with insulin-sensitizing activities. This agent had been used efficiently in a large number of patients but was withdrawn from the market in March 2000 because of its association with idiosyncratic hepatotoxicity. To address the susceptible genetic factors responsible for the hepatotoxicity associated with this agent, we performed a genetic polymorphic analysis by a target gene approach in troglitazone-treated Japanese patients with type 2 diabetes mellitus. Methods: One hundred ten patients treated with troglitazone were recruited into this study. The case patients (n = 25) were recruited through medical professionals who had previously reported abnormal increases in the levels of ALT or AST among their patients. The control patients (n = 85) were recruited through physicians prescribing troglitazone. For statistical accuracy, efforts were made to maximize the size of the case group. Genotype analysis was performed in 68 polymorphic sites of 51 candidate genes related to drug metabolism, apoptosis, production and elimination of reactive oxygen species, and signal transduction pathways of peroxisome proliferator-activated receptor gamma 2 and insulin. Results: The strong correlation with transaminase elevations was observed in the combined glutathione-S-transferase GSTT1-GSTM1 null genotype (odds ratio, 3.692; 95% confidence interval, 1.354-10.066; P = .008). Conclusions: The double null mutation of GSTT1 and GSTM1 might influence troglitazone-associated abnormal increases of liver enzyme levels.

L232 ANSWER 13 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003076287 EMBASE
TITLE: PTP1B inhibitors as potential therapeutics in the treatment of type 2 diabetes and obesity.
AUTHOR: Zhang Z.-Y.; Lee S.-Y.
CORPORATE SOURCE: Z.-Y. Zhang, Department of Molecular Pharmacology, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, United States. zyzhang@aecom.yu.edu
SOURCE: Expert Opinion on Investigational Drugs, (1 Feb 2003) 12/2 (223-233).
Refs: 84
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Coordinated tyrosine phosphorylation is essential for signalling pathways regulated by insulin and leptin. Type 2 diabetes and obesity are characterised by resistance to hormones insulin and leptin, possibly due to attenuated or diminished signalling from the receptors. Pharmacological agents capable of inhibiting the negative regulator(s) of the signalling pathways are expected to potentiate the action of insulin and leptin and therefore be beneficial for the treatment of Type 2 diabetes and obesity. A large body of data from cellular, biochemical, mouse and human genetic and chemical inhibitor studies have identified protein tyrosine phosphatase 1B (PTP1B) as a major negative regulator of both insulin and leptin signalling. In addition, evidence suggests that insulin and leptin action can be enhanced by the inhibition of PTP1B. Consequently, PTP1B has emerged as an attractive novel target for the treatment of both Type 2 diabetes and obesity. The link between PTP1B and diabetes and obesity has led to an avalanche of research dedicated to finding inhibitors of this phosphatase. With the combined use of structure and medicinal chemistry, several groups have demonstrated that it is feasible to obtain small-molecule PTP1B inhibitors with the requisite potency and selectivity. The challenge for the future will be to transform potent and

selective small molecule PTP1B inhibitors into orally available drugs with desirable physicochemical properties and in vivo efficacies.

L232 ANSWER 14 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003036942 EMBASE
TITLE: Therapeutic potential of dipeptidyl peptidase IV inhibitors for the treatment of type 2 diabetes.
AUTHOR: Drucker D.J.
CORPORATE SOURCE: D.J. Drucker, Banting and Best Diabetes Centre, Toronto General Hospital, University of Toronto, 200 Elizabeth Street MBRW4R-902, Toronto, Ont. M5G 2C4, Canada. d.drucker@utoronto.ca
SOURCE: Expert Opinion on Investigational Drugs, (1 Jan 2003) 12/1 (87-100).
Refs: 159
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Incretins are peptide hormones, exemplified by glucose-dependent insulinotropic peptide and glucagon-like peptide 1 that are released from the gut in response to nutrient ingestion and enhance glucose-stimulated insulin secretion. Incretin action is terminated due to N-terminal cleavage of the peptides by the aminopeptidase dipeptidyl peptidase IV (DPP-IV). Hence, inhibition of glucose-dependent insulinotropic peptide and glucagon-like peptide 1 degradation via reduction of DPP-IV activity represents an innovative strategy for enhancing incretin action in vivo. This review summarises the biology of incretin action, the structure, expression and pleiotropic biological activities of DPP-IV and provides an overview of the rationale, potential merits and theoretical pitfalls in the development of DPP-IV inhibitors for the treatment of type 2 diabetes.

L232 ANSWER 15 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002423939 EMBASE
TITLE: Biomarkers and functional foods for obesity and diabetes.
AUTHOR: Hill J.O.; Peters J.C.
CORPORATE SOURCE: Dr. J.O. Hill, Center for Human Nutrition, University of Colorado, Health Sciences Center, 4200 East Ninth Avenue, Denver, CO 80262, United States. james.hill@uchsc.edu
SOURCE: British Journal of Nutrition, (1 Nov 2002) 88/SUPPL. 2 (S213-S218).
Refs: 47
ISSN: 0007-1145 CODEN: BJNUAV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
017 Public Health, Social Medicine and Epidemiology
003 Endocrinology
005 General Pathology and Pathological Anatomy
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Obesity has reached epidemic proportions in many countries around the world. Because of the close relationship between obesity and type 2

diabetes, an epidemic of diabetes is close behind the obesity epidemic. Preventing and treating obesity is becoming an increasing priority. In the United States, over 60% of the adult population is overweight or obese and thus at increased risk of developing diabetes and cardiovascular disease. While the aetiology of obesity and diabetes is complex, diet clearly plays an important role both in the development and management of these diseases. There is interest in functional foods that could help in prevention and/or management of obesity and type 2 diabetes. This could involve food products that help management of 'hunger' or that increase 'satiety'. It could also involve foods that contribute to more inefficient use of ingested energy (i.e. foods that stimulate energy expenditure more than would be expected from their energy content). As the concept of insulin sensitivity becomes generally more accepted by health care professionals and the public, foods may be targeted towards maximizing insulin sensitivity and towards 'prevention' of diabetes. In addition to foods that impact upon body weight, these may include foods that affect the glucose and/or insulin levels that are seen either following the ingestion of food or later in the day. The present paper reviews the complex aetiology of obesity and diabetes and considers a potential role for functional foods in prevention and treatment of obesity and diabetes.

L232 ANSWER 16 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002028481 EMBASE
TITLE: Endocrinology.
AUTHOR: Burgess J.R.
CORPORATE SOURCE: Dr. J.T. Burgess, Dept. of Diabetes and Endocrinology, Royal Hobart Hospital, Hobart, Tas., Australia. jburges@utas.edu.au
SOURCE: Medical Journal of Australia, (7 Jan 2002) 176/1 (12). Refs: 2
ISSN: 0025-729X CODEN: MJAUAJ
COUNTRY: Australia
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
030 Pharmacology
029 Clinical Biochemistry
036 Health Policy, Economics and Management
026 Immunology, Serology and Transplantation
048 Gastroenterology
009 Surgery
039 Pharmacy
022 Human Genetics
LANGUAGE: English

L232 ANSWER 17 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001302760 EMBASE
TITLE: Carbohydrate and fat metabolism and related hormonal regulation in normal and diabetic placenta.
AUTHOR: Hauguel-de Mouzon S.; Shafrir E.
CORPORATE SOURCE: E. Shafrir, Department of Biochemistry, Hadassah University Hospital, Kiryat Hadassah p.o.b. 12000, IL-91120 Jerusalem, Israel
SOURCE: Placenta, (2001) 22/7 (619-627). Refs: 117
ISSN: 0143-4004 CODEN: PLACDF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: English

L232 ANSWER 18 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001302554 EMBASE
TITLE: Insulin resistance and .beta.-cell dysfunction as therapeutic targets in type 2 diabetes.
AUTHOR: Evans A.J.; Krentz A.J.
CORPORATE SOURCE: Dr. A. Krentz, Southampton General Hospital, Southampton SO16 6YD, United Kingdom. a.j.krentz@soton.ac.uk
SOURCE: Diabetes, Obesity and Metabolism, (2001) 3/4 (219-229).
Refs: 70
ISSN: 1462-8902 CODEN: DOMEF6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L232 ANSWER 19 OF 20 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000048451 EMBASE
TITLE: Effects of streptozotocin-induced diabetes and insulin treatment on the hypothalamic melanocortin system and muscle uncoupling protein 3 expression in rats.
AUTHOR: Hayel P.J.; Hahn T.M.; Sindelar D.K.; Baskin D.G.; Dallman M.F.; Weigle D.S.; Schwartz M.W.
CORPORATE SOURCE: Dr. P.J. Hayel, Department of Nutrition, University of California, One Shields Ave., Davis, CA 95616, United States. pjhavel@ucdavis.edu
SOURCE: Diabetes, (2000) 49/2 (244-252).
Refs: 72
ISSN: 0012-1797 CODEN: DIAEAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hypothalamic melanocortins are among several neuropeptides strongly implicated in the control of food intake. Agonists for melanocortin 4 (MC-4) receptors such as .alpha.-melanocyte-stimulating hormone (.alpha.-MSH), a product of proopiomelanocortin (POMC), reduce food intake, whereas hypothalamic agouti- related protein (AgRP) is a MC-4 receptor antagonist that increases food intake. To investigate whether reduced melanocortin signaling contributes to hyperphagia induced by uncontrolled diabetes, male Sprague-Dawley rats were studied 7 days after administration of streptozotocin (STZ) or vehicle. In addition, we wished to determine the effect of diabetes on muscle uncoupling protein 3 (UCP3), a potential regulator of muscle energy metabolism. STZ diabetic rats were markedly hyperglycemic (31.3 .+-. 1.0 mmol/l; P < 0.005) compared with nondiabetic controls (9.3 .+-. 0.2 mmol/l). Insulin treatment partially corrected the hyperglycemia (18.8 .+-. 2.5 mol/l; P < 0.005). Plasma leptin was markedly reduced in STZ diabetic rats (0.4 .+-. 0.1 ng/ml; P < 0.005) compared with controls (3.0 .+-. 0.4 ng/ml), an effect that was also partially reversed by insulin treatment (1.8 .+-. 0.3 ng/ml). Untreated diabetic rats were hyperphagic, consuming 40% more food (48 .+-. 1 g/day; P < 0.005) than controls (34 .+-. 1 g/day). Hyperphagia was prevented by insulin treatment (32 .+-. 2 g/day). In untreated diabetic rats, hypothalamic POMC mRNA expression (measured by in situ hybridization) was reduced by 80% (P < 0.005), whereas AgRP mRNA levels were increased by 60% (P < 0.01), suggesting a marked decrease of

hypothalamic melanocortin signaling. The change in POMC, but not in AgRP, mRNA levels was partially reversed by insulin treatment. By comparison, the effects of diabetes to increase hypothalamic neuropeptide Y (NPY) expression and to decrease corticotropin-releasing hormone (CRH) expression were normalized by insulin treatment, whereas the expression of mRNA encoding the long form of the leptin receptor in the arcuate nucleus was unaltered by diabetes or insulin treatment. UCP-3 mRNA expression in gastrocnemius muscle from diabetic rats was increased fourfold ($P < 0.005$), and the increase was prevented by insulin treatment. The effect of uncontrolled diabetes to decrease POMC, while increasing AgRP gene expression, suggests that reduced hypothalamic melanocortin signaling, along with increased NPY and decreased CRH signaling, could contribute to diabetic hyperphagia. These responses in concert with increased muscle UCP-3 expression, may also contribute to the catabolic effects of uncontrolled diabetes on fuel metabolism in peripheral tissues.

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AB Type-II-diabetes is a genetically determined disease which is considerably affected by exogenous factors like diet or exercise. A crucial factor in the course of this disease is obesity, leading to insulin resistance and exhaustion of the insulin-secreting cells. This review describes the recently identified obesity genes and discusses their relevance for the human disease. Adipose stores are mainly balanced by the hormone leptin. Lack of leptin or of its receptor leads to a rare syndrome of extreme hyperphagia, obesity, reduced thermogenesis and insulin resistance. However, the majority of obese patients, and also several mouse strains with polygenic obesity and insulin resistance, exhibit leptin resistance. This syndrome is due to the combined effect of several yet unidentified genes involved in leptin and insulin signaling.

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